BIPMed - Brazilian Initiative on Precision Medicine

www.bipmed.org

Precision Medicine

Current medical practice

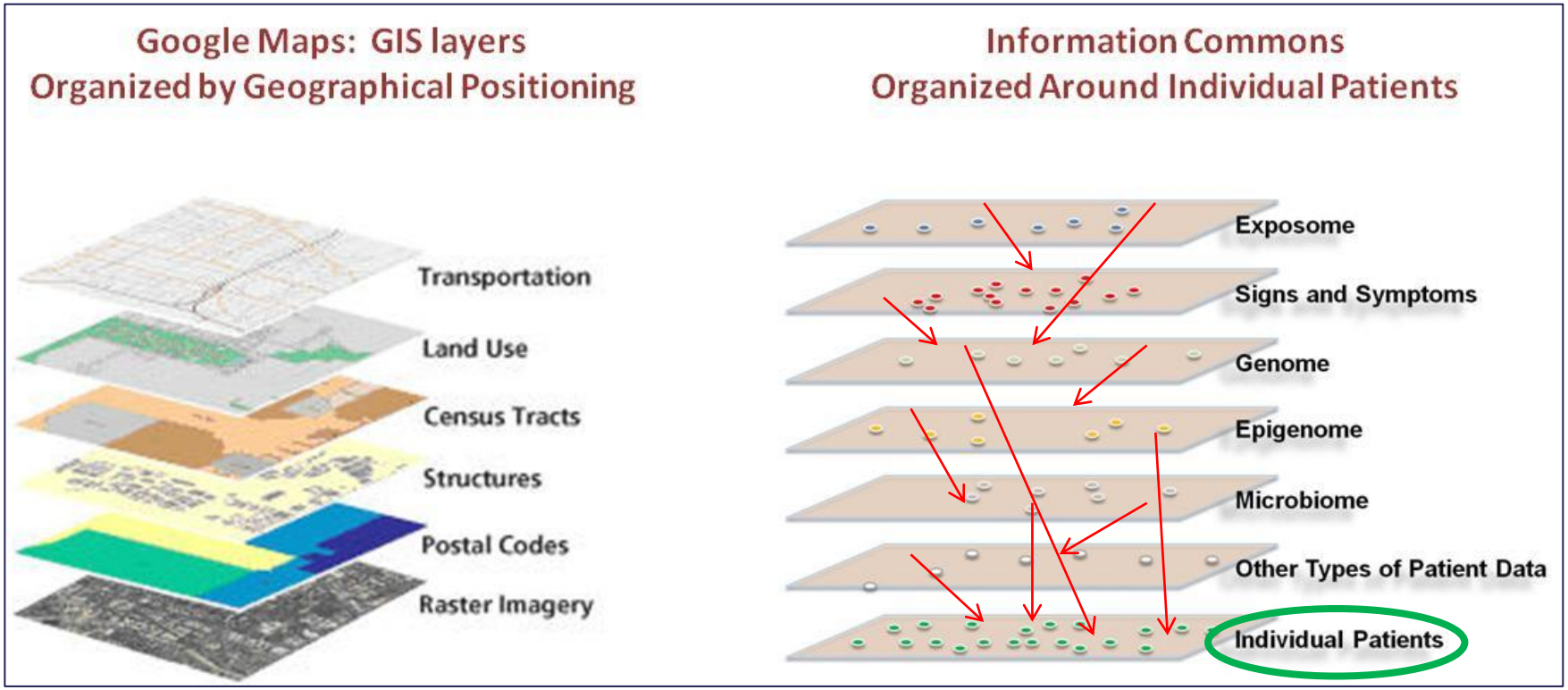
Use vital signs today relative to last visit; assess symptoms; physician uses expert background, experience and judgment to diagnose and prescribe

Precision medicine

Use massive data network that aggregates and analyzes information from huge patient cohorts, healthy populations, experimental organisms – and reaches toward disease mechanisms, and precision diagnosis and treatment for each individual

Modified from:Yamamoto et al. 2014

Precision Medicine



Yamamoto et al. 2014

Precision Medicine

- Diverse data types: *e.g., -omics, imaging (e.g., brain activity, longitudinal MRI), population studies, environmental effects.*
- Digital health: *wearable sensors (biosensors): COLLECT LARGE AMOUNT OF DATA*
- Data acquisition, aggregation, integration, analysis
- Data storage, security, selective access
- Data sorting and visualization
- **Data sharing**

Modified from:Yamamoto et al. 2014

FAPESP

BIPMed Brazilian Initiative on Precision Medicine

SAVE THE DATE

The São Paulo Research Foundation, FAPESP, under the scope of the program Research, Innovation and Dissemination Centers (RIDCs), invite you to the

Launching of the

BRAZILIAN INITIATIVE ON PRECISION MEDICINE

BIPMed

November, 13, 2015
1:30pm to 5:00pm
Venue: FAPESP - Rua Pio XI, 1500
Alto da Lapa – São Paulo

Partnership

Global Alliance for Genomics & Health

Supported by

affymetrix illumina

Support


BIPMed
Brazilian Initiative on
PRECISION MEDICINE


UNICAMP
BRAIN
BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY


eScience
UNICAMP


CTC
CENTRO DE TERAPIA CELULAR
CENTER FOR CELL-BASED THERAPY


CRID


OCRC
Obesity and
Comorbidities
Research Center


Global Alliance
for Genomics & Health


THE
HUMAN VARIOME
PROJECT


FAPESP

Mission

- To help implement precision medicine in Brazil by acting as a catalytic element to foster collaboration among different stake holders (scientist, physicians, health authorities, hospitals, society)

First product: BIPMed genomic database

Global Alliance for Genomics & Health

Collaborate. Innovate. Accelerate.

National Initiatives 'Pre-Meeting' at GA4GH 4th Plenary - Agenda

Date: October 17, 2016
Time: 1-3pm PDT | 8-10pm UTC
Location: 'Ambleside 2' room at Vancouver Marriott Pinnacle Downtown Hotel
1128 W Hastings St., Vancouver, Canada
Contact: Lena Dolman (lena.dolman@genomicsandhealth.org)

Attendees:

- GA4GH: Kathryn North, Peter Goodhand, Julia Wilson, Lena Dolman
- Australia and AGHA: Sean Grimmond, John Christodoulou, Andrew Sinclair, Marcel Dinger, Clara Gaff, Sylvia Metcalfe, Oliver Hofmann
- Genomics England: Augusto Rendon, Mark Caulfield
- Genome Canada: Cindy Bell, Kate Swan
- French National Genotyping Centre: Jean-François Deleuze
- Brazilian Society of Medical Genetics: Iscia Cendes-Lopes ← BIPMed
- H3Africa: Nicola Mulder
- Cancer Moonshot blue ribbon panel: Angel Pizarro
- Precision Medicine Initiative: David Glazer
- National Cancer Centre of Singapore: Bin Tean Teh (via Zoom)

GENOMICS

A federated ecosystem for sharing genomic, clinical data

Silos of genome data collection are being transformed into seamlessly connected, independent systems

The Global Alliance for Genomics and Health*

Early data-sharing efforts have led to improved variant interpretation and development of treatments for rare diseases and some cancer types (*1*–*3*). However, such benefits will only be available to the general population if researchers and clinicians can access and make comparisons across data from millions of individuals.

POLICY

Despite much progress, genomic and clinical data are still generally collected and studied in silos: by disease, by institution, and by country. Regulatory data-privacy requirements do not seamlessly lend themselves to the secure sharing of data within and across institutions and countries (*4*). Current practices in research and medicine hinder the sharing of data in ways that tangibly recognize an individual's contributions. Tools and analytical methods are nonstandardized and incompatible, and the data are often stored in incompatible file formats.

Science
AAAS

A federated ecosystem for sharing genomic, clinical data

The Global Alliance for Genomics and Health (June 9, 2016)
Science **352** (6291), 1278-1280. [doi: 10.1126/science.aaf6162]

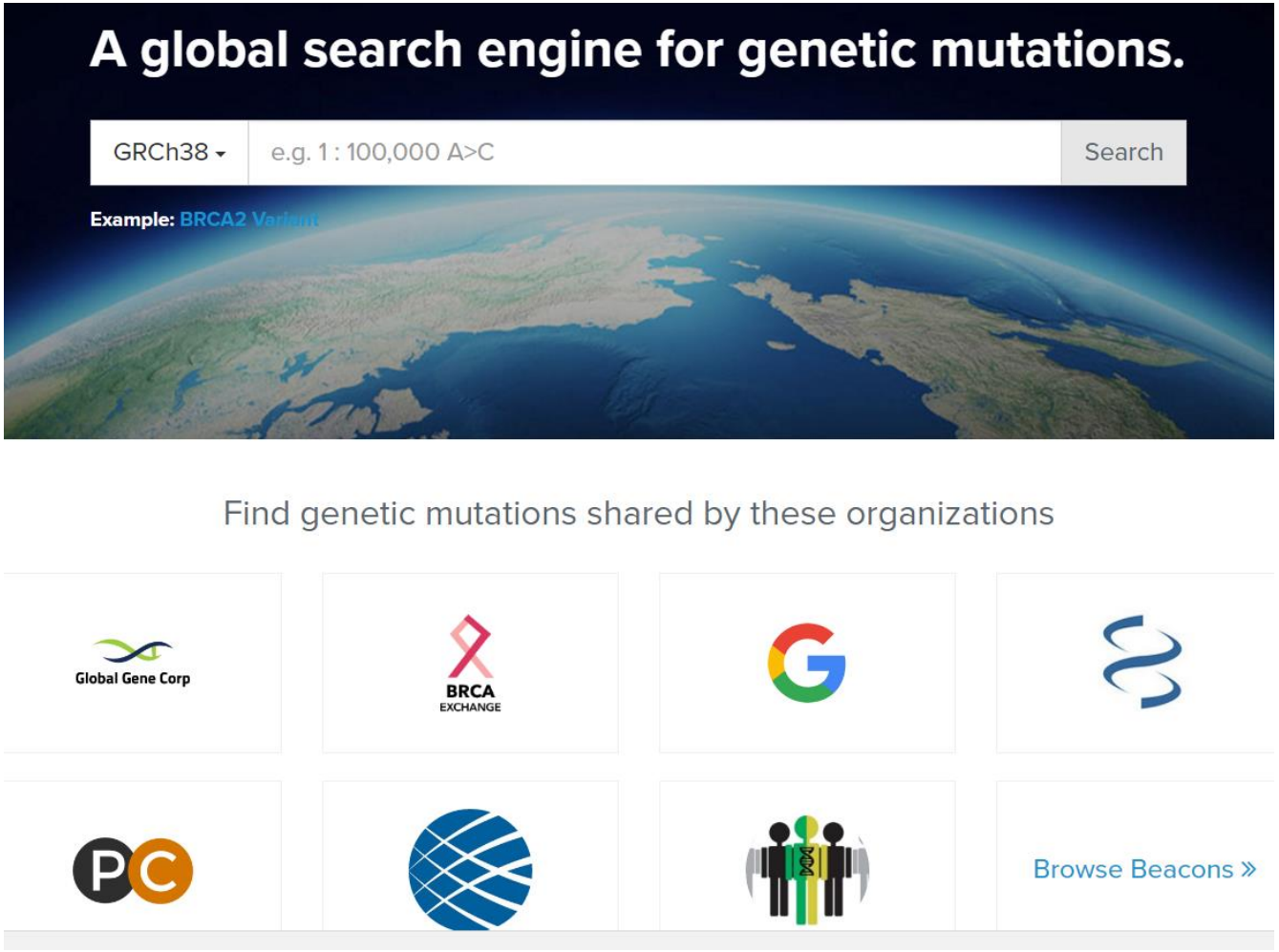
REMAINING CHALLENGES. Shringarpure and Bustamante (*11*) used simulations to show that, in some scenarios, querying a public beacon for as few as 250 variants already known to be present in an individual's genome could reveal information distinctive to that individual. GA4GH members have been developing solutions to this potential security breach since the project's inception, including aggregating data among multiple beacons, tracking usage to restrict systematic searches and introducing tiers of secured access that require users to be authorized for data access—but these necessarily limit the scope of information that can be shared widely. Innovative policy and regulatory measures, as well as technological solutions, are needed to securely handle individual genomic and clinical data.

Finally, ensuring engagement among the entire global community is necessary from a social justice and medical perspective, although this will likely require distinct legal, cultural, and business models. In some countries, health care and research organizations are interested in GA4GH as a means to link nascent national efforts in precision medicine with other international groups, such as the Brazilian Initiative on Precision Medicine (www.fcm.unicamp.br/gtc/evento/1/trabalho/8).

BIPMed Brazilian Initiative on PRECISION MEDICINE

BEACON

https://beacon-network.org



Beacon Adoption

Global Alliance for Genomics & Health

60+ Beacons

250+ Datasets

60,000+ Queries

100,000+ Individual Subjects

BIPMed

Our Products:

- Genomic databases:
  - BIPMed-WES-db: REFERENCE POPULATION
  - BIPMed-Array-db: REFERENCE POPULATION
  - DISEASE SPECIFIC DATABASES
- BIPMed Beacon
- GA4GH R client

Disease/Phenotype specific projects

- Epilepsy (BRAINN, ILAE-ALADE) - EE

- Stroke (BRAINN, ISGC-Latinamerican Initiative)
- Cleft lip and palate (BCFP) – Dr. Vera Lopes
- BRCA – BRCA Challenge (GA4GH, HVP) – Dr. Patricia Prolla and Edenir Palmero
- Pathogenic hemoglobins – Global Globin (HVP) – Monica Melo
- ApoE Challenge (BRAINN, ABN) – Dr. Marcio Balthazar
- Pharmacogenomics (BRAINN, UNIFESP) – Marcelo Briones
- …….

Genomic Databases

LOVD

- Lieden Open Variation Database
- Web-based gene sequence variation database
- Freely available tool for Gene-centered collection and display of DNA variations.

Under development

- Link databases to ClinVar
- Realign the WES data with GRCh37 reference
- Use GRCh37 reference for the SNP-array database
- Use GRCh37 reference for the Epileptic Encephalopathies
- Soon launch all cohorts with two reference genomes

BIPMed

Brazilian Initiative on Precision Medicine

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QUESTIONS / SUGGESTIONS: Send us an email!

alpha-1-B glycoprotein (A1BG)

Curator: Admin

Genes | Transcripts | Variants | Diseases | Documentation

View all genes

20857 entries on 209 pages. Showing entries 1 - 100.

100 per page ▼ « First ‹ Prev 1 2 3 4 5 6 7 8 9 10 11 ... Next › Last »

Symbol	Gene	Chr	Band	Transcripts	Variants	Unique variants	Last updated	Associated with diseases
A1BG	alpha-1-B glycoprotein	19	q13.43	1	148	0	2015-12-17	-
A1BG-AS1	A1BG antisense RNA 1	19	q13.43	1	192	1	2015-12-17	-
A1CF	APOBEC1 complementation factor	10	q21.1	10	109	2	2015-12-26	-
A2M	alpha-2-macroglobulin	12	p13.31	2	304	0	2015-12-26	-
A2M-AS1	A2M antisense RNA 1 (head to head)	12	p13.31	1	22	0	2015-12-15	-
A2ML1	alpha-2-macroglobulin-like 1	12	p13	4	455	1	2015-12-26	-
A2MP1	alpha-2-macroglobulin pseudogene 1	12	p13.31	1	2	0	2015-12-15	-
A3GALT2	alpha 1,3-galactosyltransferase 2	1	p35.1	1	9	6	2015-12-13	-
A4GALT	alpha 1,4-galactosyltransferase	22	q13.2	10	147	3	2015-12-26	-
A4GNT	alpha-1,4-N-acetylglucosaminyltransferase	3	p14.3	1	107	6	2015-12-19	-
AAAS	achalasia, adrenocortical insufficiency, alacrimia	12	q13	9	200	3	2015-12-15	-
AACS	acetoacetyl-CoA synthetase	12	q24.31	5	127	6	2015-12-14	-
AACSP1	acetoacetyl-CoA synthetase pseudogene 1	5	q35	1	163	2	2015-12-26	-
AADAC	arylacetamide deacetylase	3	q25.1	2	249	16	2015-12-26	-
AADACL2	arylacetamide deacetylase-like 2	3	q25.1	2	64	9	2015-12-19	-
AADACL2-AS1	AADACL2 antisense RNA 1	3	q25.1	0	0	0	2016-03-16	-
AADACL3	arylacetamide deacetylase-like 3	1	p36.21	2	190	13	2015-12-07	-
AADACL4	arylacetamide deacetylase-like 4	1	p36.21	5	13	0	2015-12-12	-
AADAT	aminoadipate aminotransferase	4	q33	6	69	2	2015-12-26	-
AAED1	AhpC/TSA antioxidant enzyme domain containing 1	9	q22.32	3	1	0	2015-12-03	-
AAGAB	alpha- and gamma-adaptin binding protein	15	q23	6	138	3	2015-12-16	-
AAK1	AP2 associated kinase 1	2	p13.3	1	346	0	2015-12-26	-
AAMDC	adipogenesis associated, Mth938 domain containing	11	q14.1	4	46	2	2015-12-14	-
AAMP	angio-associated migratory cell protein	2	q	2	30	1	2015-12-07	-
AANAT	aralkylamine N-acetyltransferase	17	q25.1	9	37	5	2015-12-26	-
AAR2	AAR2 splicing factor homolog	20	q11.23	5	9	0	2015-12-18	-
AARD	alanine and arginine rich domain containing protein	8	q24.11	2	15	0	2015-12-24	-

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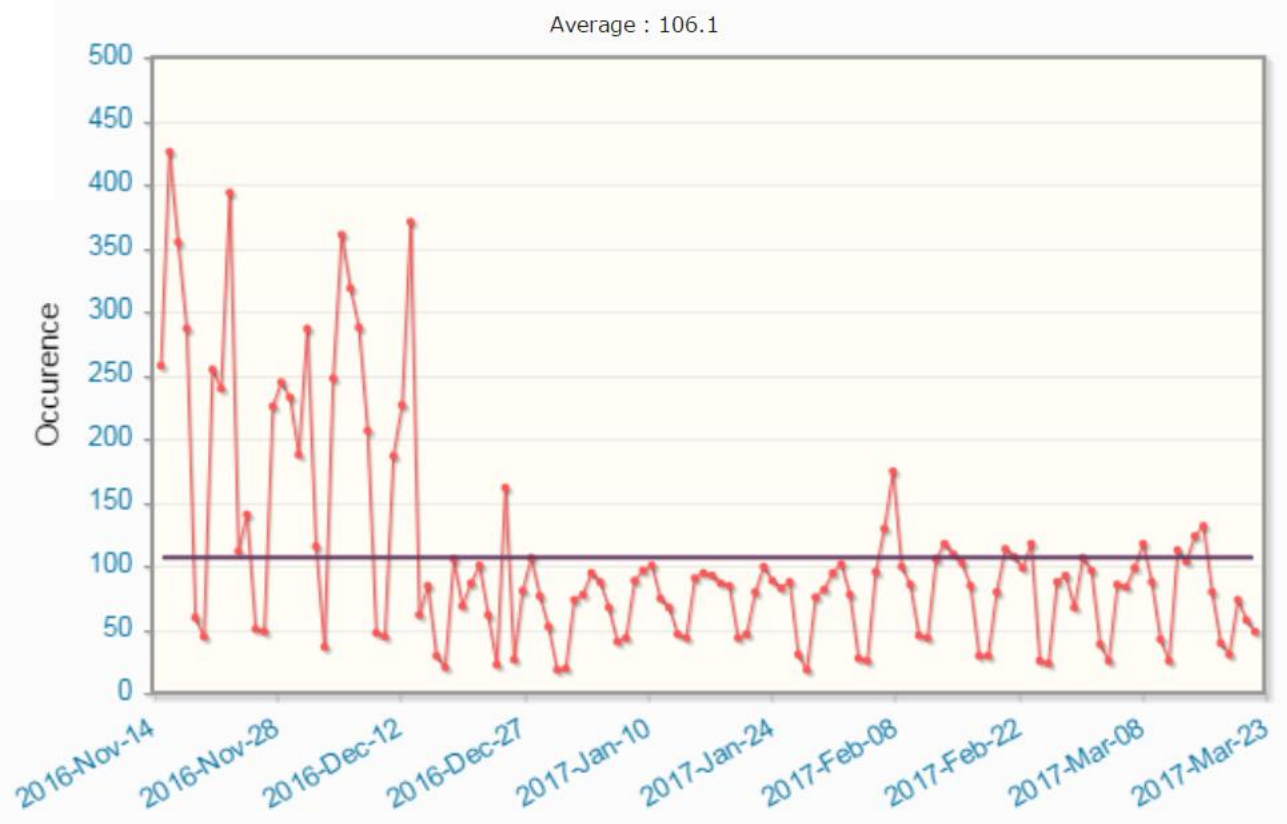
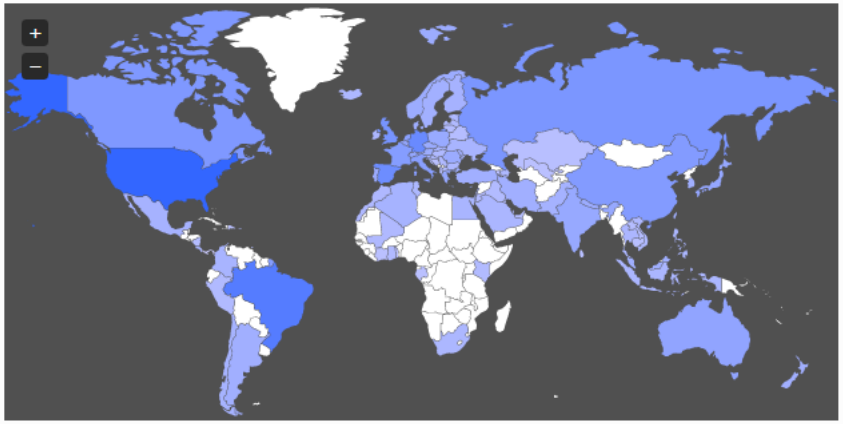
Access Statistics



BIPMed Brazilian Initiative on PRECISION MEDICINE

Access Statistics



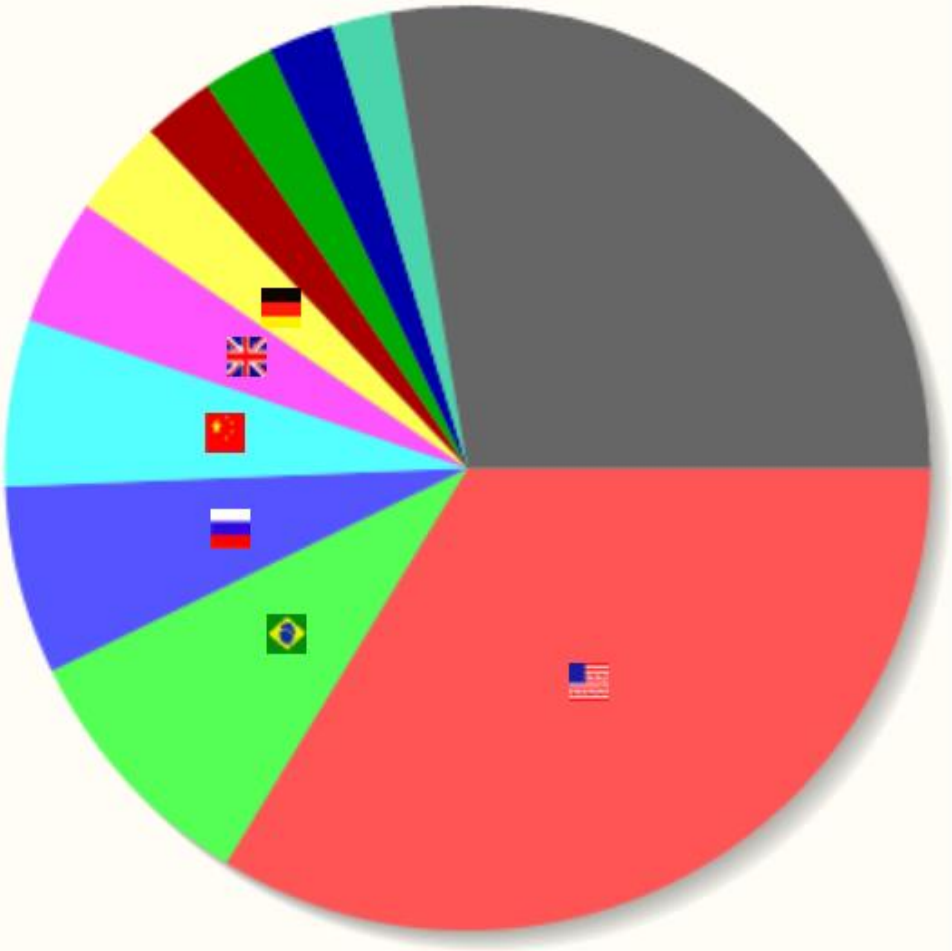
Requests | Accesses | Hosts Traffic

	Hosts	Percentage	Requests	Percentage	Accesses	Percentage	Traffic (Mb)	Percentage
North-America	1027	35.4 %	89483	46.9 %	51355	57.3 %	4789.1	55.8 %
Europe	982	33.9 %	56718	29.7 %	20363	22.7 %	2944.5	34.3 %
South-America	297	10.2 %	29902	15.7 %	14575	16.3 %	492.4	5.7 %
Asia	477	16.5 %	11577	6.1 %	2645	2.9 %	273.5	3.2 %
Oceania	42	1.4 %	2007	1.1 %	522	0.6 %	58.7	0.7 %
Africa	56	1.9 %	674	0.4 %	164	0.2 %	18.8	0.2 %
Central-America	15	0.5 %	322	0.2 %	59	0.1 %	8.2	0.1 %
Misc	3	0.1 %	44	0.0 %	9	0.0 %	2.1	0.0 %

BIPMed Brazilian Initiative on PRECISION MEDICINE

Access Statistics

Countries		
United States -	978	33.7 %
Brazil -	262	9.0 %
Russian Federation -	191	6.5 %
China -	169	5.8 %
Great Britain -	128	4.4 %
Germany -	98	3.3 %
Italy -	73	2.5 %
France -	72	2.4 %
India -	66	2.2 %
Spain -	59	2.0 %
Others	803	27.6 %



LEVELS OF ACCESS OF GENOMIC INFORMATION DEPOSITED IN THE BIPMED PUBLIC GENOMIC DATABASE

Level 1 or Unrestricted Access: This is the standard access level and it does not require user registration or authentication. Users can access polled statistics, list of variants; frequency. **Users do not have access to individualized data.**

Level 2 or Restricted Access: It requires registration and users can request access to files containing specific datasets. Registered users must sign a *Data Sharing Agreement*, which includes a confidentiality clause. Registered users can request Individual VCF files containing variants information.

Bottleneck Server – a.k.a. IP Throttling

Beacon slows down requests, if too many come from the same IP. This prevents whole-genome queries for all alleles. This control is done by a “Bottleneck Server”;

Every time someone asks the Beacon one question, the Beacon asks the Bottleneck Server how many questions you already asked in the past and how long ago was the last question;

If you asked (N+1) questions and waited K seconds between questions N and (N+1), then you will get an answer after (150N-10K) ms;

If the wait time exceeds 20s, your IP will be blocked for a while and the answers will be much slower after your IP is unblocked.

PLOS ONE

RESEARCH ARTICLE

A Prediction Algorithm for Drug Response in Patients with Mesial Temporal Lobe Epilepsy Based on Clinical and Genetic Information

Mariana S. Silva-Alves[1☯], Rodrigo Secolin[1☯], Benilton S. Carvalho[2], Clarissa L. Yasuda[3], Elizabeth Bilevicius[3], Marina K. M. Alvim[3], Renato O. Santos[1], Claudia V. Maurer-Morelli[1], Fernando Cendes[3], Iscia Lopes-Cendes[1]*

1 Department of Medical Genetics, University of Campinas—UNICAMP, and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, São Paulo, Brazil, **2** Department of Statistics, Institute of Mathematics, Statistics and Scientific Computing, University of Campinas—UNICAMP, and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, São Paulo, Brazil, **3** Department of Neurology, University of Campinas—UNICAMP, and the Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, São Paulo, Brazil

☯ These authors contributed equally to this work.
* icendes@unicamp.br

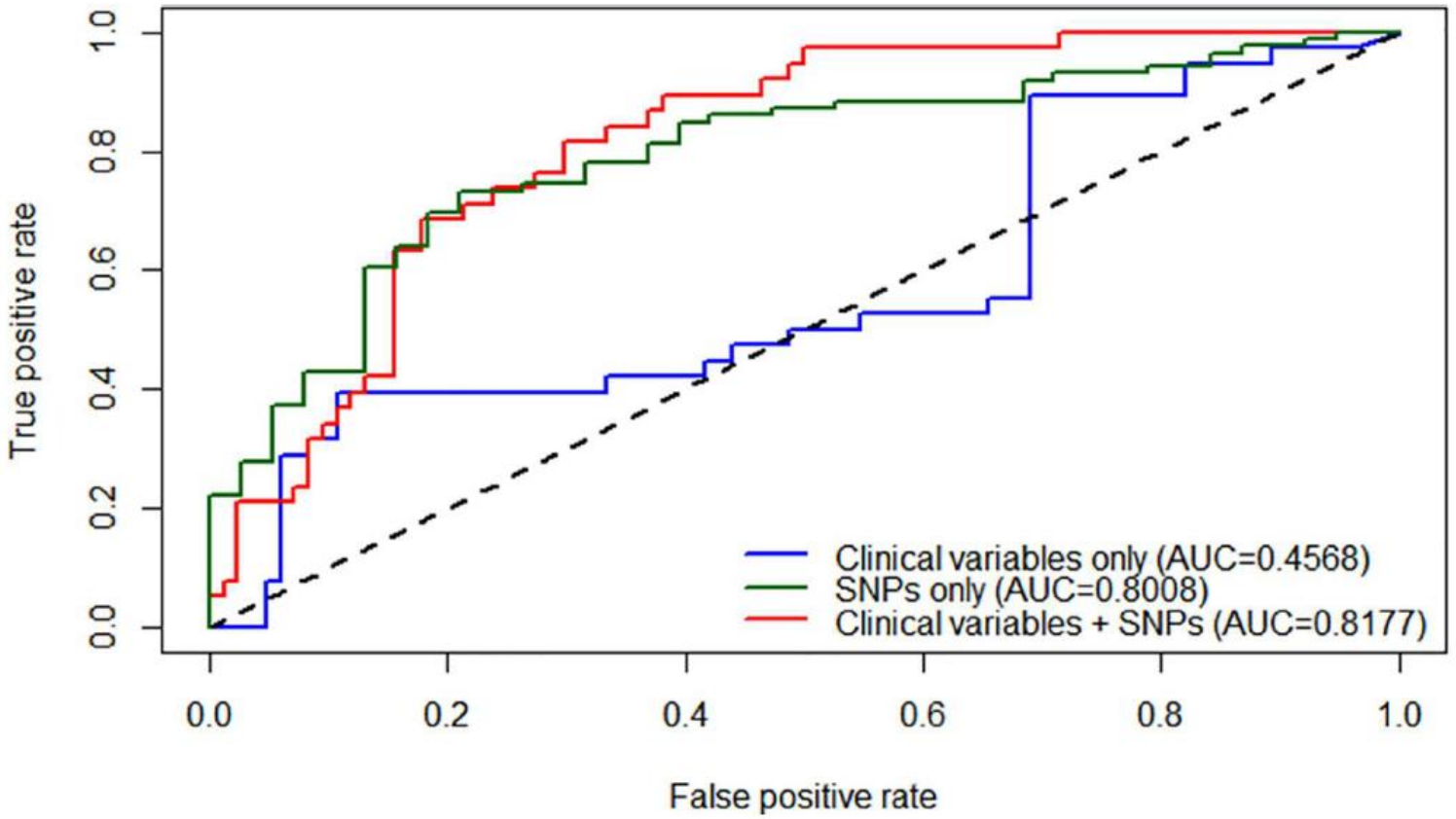
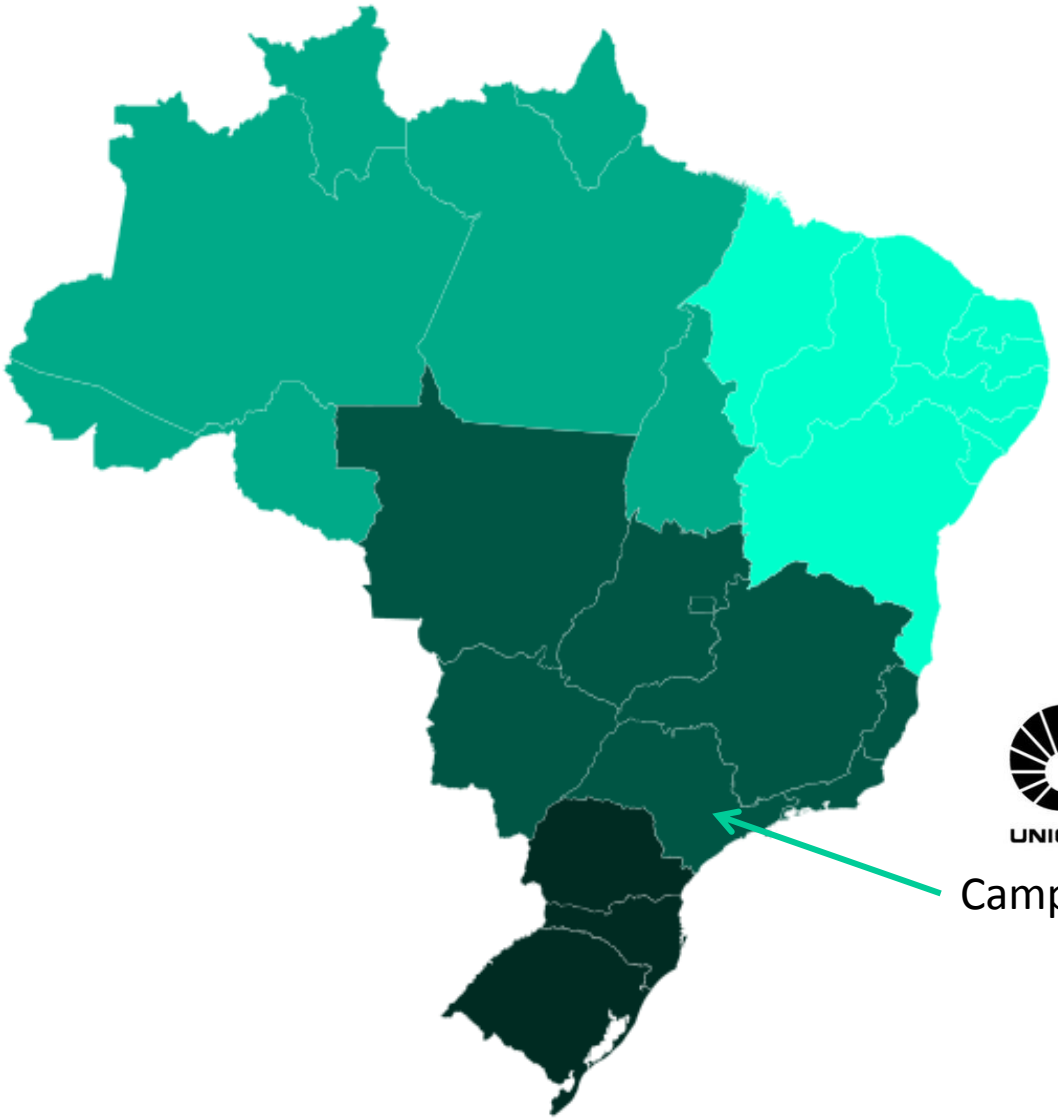


Fig 2. ROC curve showing the true positive rate (sensitivity), in function of false positive rate (1-specificity). The blue line indicates the prediction scenario using only clinical variables (hippocampal sclerosis, age of onset epilepsy, febrile seizures, and gender). The red line indicates the second scenario using the clinical variables plus SNPs. The dark green line indicates the scenario using only SNP genotypes. The area under the curve (AUC) values is showed for the three scenarios. The diagonal dashed line indicates a non-informative prediction (AUC = 0.5).



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UNICAMP

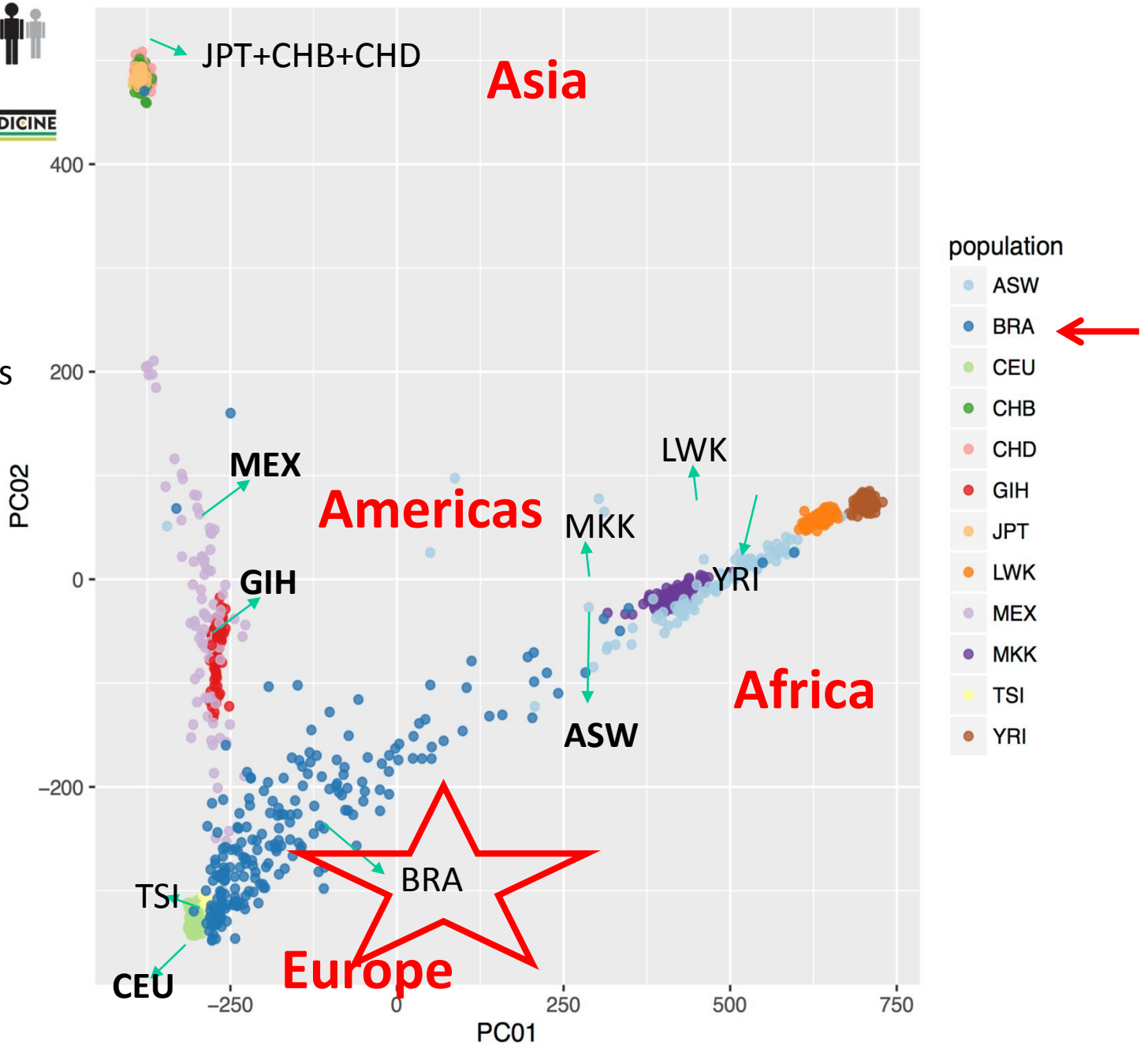
Campinas, SP

Reference Individuals

BIPMed
SNP-arrays
196 individuals

x

HapMap



Ananina G et al. 2016
submitted

Fine scale genetic structure of the populations from three Brazilian regions

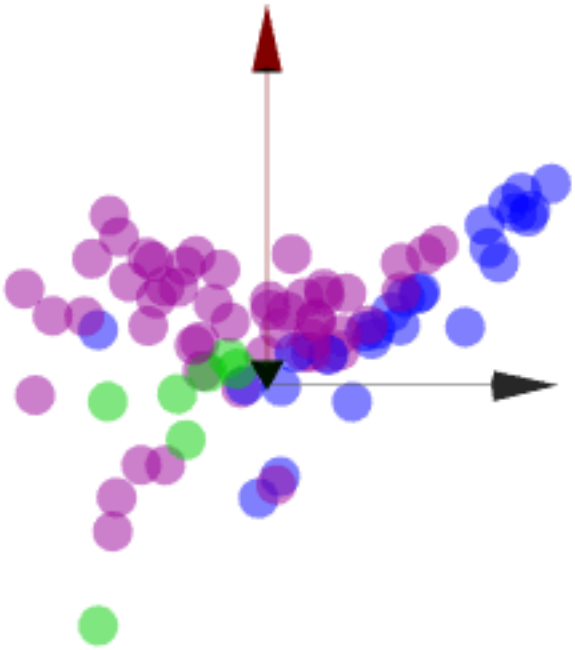
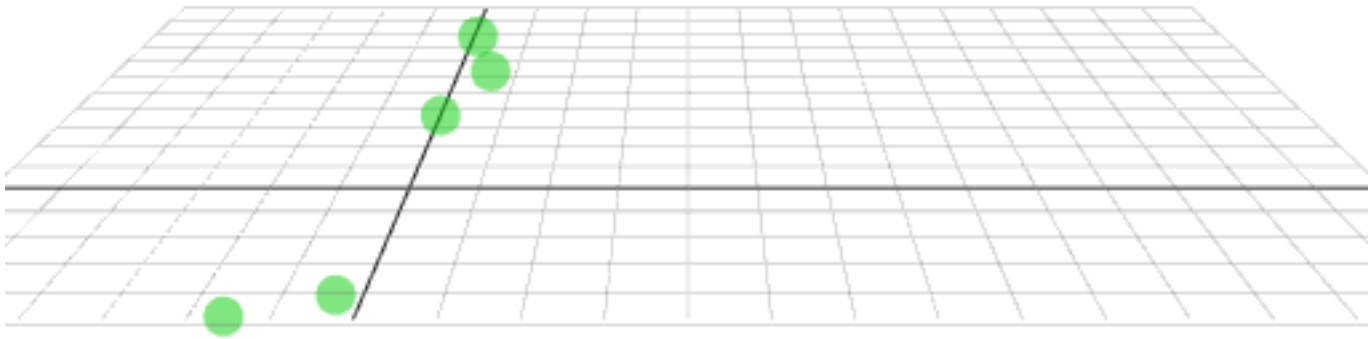
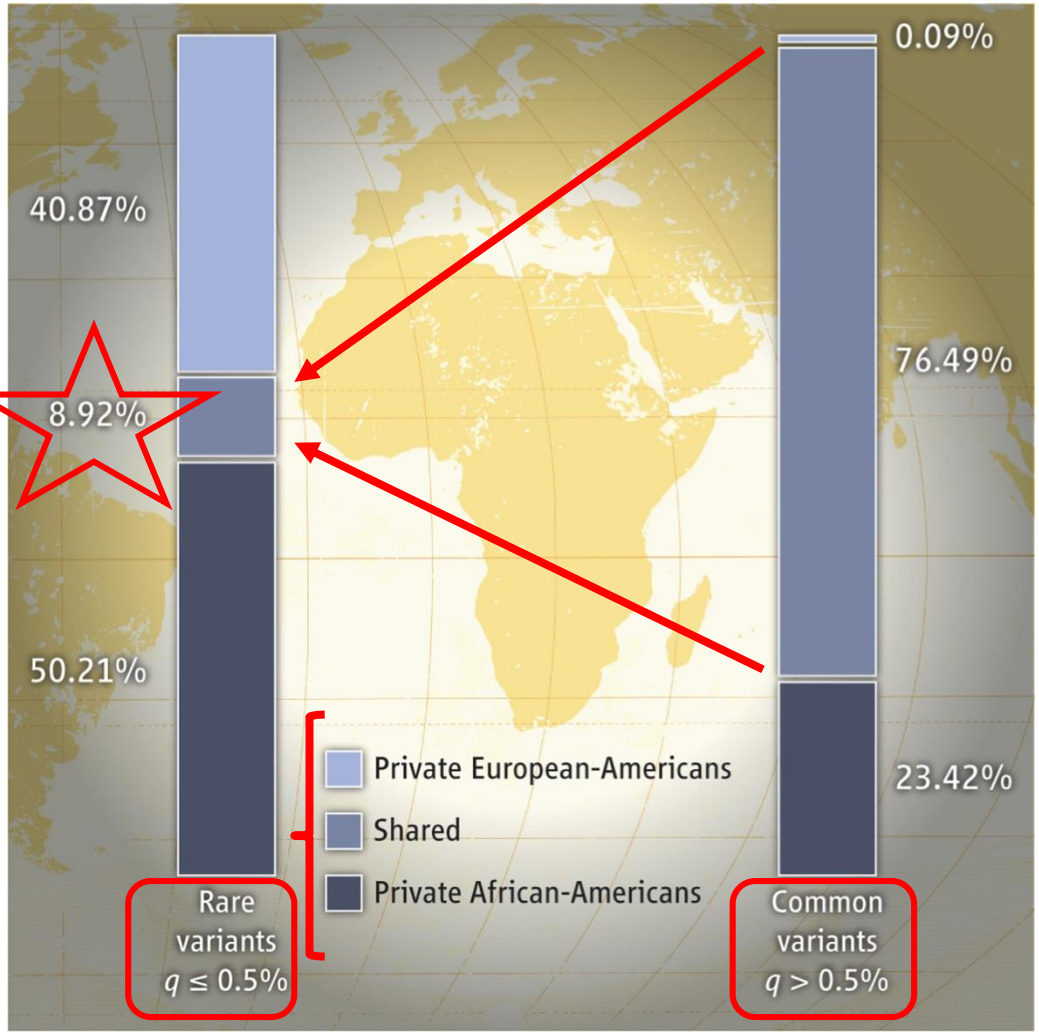


Gráfico de Componentes Principais: PC1 x PC2 x PC3

Recife, PE ←
Campinas, SP ←
Joinville,SP ←



Human genetic variation.Proportion of shared and unshared (private) variants between the African-American and the European-American populations [data from (1)].



Ferran Casals, and Jaume Bertranpetit Science 2012;337:39-40

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Acta Neurologica Scandinavica

Acta Neurol Scand DOI: 10.1111/ane.12579

ACTA NEUROLOGICA SCANDINAVICA

DYSTONIA

New *THAP1* mutation and role of putative modifier in *TOR1A*

Piovesana LG, Torres FR, Azevedo PC, Amaral TP, Lopes-Cendes I, D'Abreu A. New *THAP1* mutation and role of putative modifier in *TOR1A*.
Acta Neurol Scand: DOI: 10.1111/ane.12579

L. G. Piovesana[1], F. R. Torres[2], P. C. Azevedo[1], T. P. Amaral[2], I. Lopes-Cendes[2], A. D'Abreu[1]

[1]Department of Neurology, University of Campinas (UNICAMP), Campinas, SP, Brazil; [2]Department of Medical Genetics, University of Campinas (UNICAMP), Campinas, SP, Brazil

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BRAIN
BRAZILIAN INSTITUTE OF NEUROSCIENCE AND NEUROTECHNOLOGY

In conclusion, our results indicate that although patients with dystonia in Brazil have clinical presentations similar to patients worldwide, the relative frequency of potentially deleterious mutations in *TORIA* and *THAP1* is low. Interestingly, considering the results from our study as well as all studies performed previously in other Brazilian patients with dystonia, the frequency of DYT6 is higher than DYT1. These findings are relevant in clinical practice, since they are in conflict with the international recommendations for the genetic diagnosis of inherited isolated dystonia. Further studies, including samples from other Brazilian regions, as well as studies of additional genes recently implicated in dystonia may better answer which algorithm would be more appropriate for genetic testing of patients with dystonia in the Brazilian population.

ELSEVIER

Cancer Genetics ■■ (2016) ■■–■■

Cancer Genetics

ORIGINAL ARTICLE

Prevalence of Hispanic *BRCA1* and *BRCA2* mutations among hereditary breast and ovarian cancer patients from Brazil reveals differences among Latin American populations

Bárbara Alemar [a,b], Josef Herzog [c], Cristina Brinckmann Oliveira Netto [d], Osvaldo Artigalás [e], Ida Vanessa D. Schwartz [a,d,f], Camila Matzenbacher Bittar [a], Patricia Ashton-Prolla [a,b,d,f,*], Jeffrey N. Weitzel [c]

GENÉTICA DE LAS ENCEFALOPATÍAS EPILÉPTICAS EN LA INFANCIA (EEI) EN AMÉRICA LATINA

Análisis molecular por secuenciación del exoma (Whole Exome Sequencing) para identificación de variantes potencialmente patogénicas.

UNICAMP

Iscia Lopes-Cendes, MD, PhD
Fernando Cendes, MD, PhD
Hebel Urquia-Osorio, PhD student

Laboratorio de Genética Molecular
Instituto Brasileiro de Neurociencias y Neurotecnología (BRAINN)
Iniciativa Brasileña de Medicina de Precisión (BIPMed)
Faculdade de Ciencias Médicas, Universidad de Campinas (UNICAMP).

INTERNATIONAL LEAGUE AGAINST EPILEPSY ILAE ESTABLISHED 1909

Conclusions

- Change in paradigm in Medicine
- Genomic Medicine is already a reality; however, to achieve Precision Medicine we need a higher level of integration of information from different sources (BIG Data)
- We are part of this global process with the launching of BIPMed, which is integrated within the GA4GH and the HVP

Lopes-Cendes laboratory

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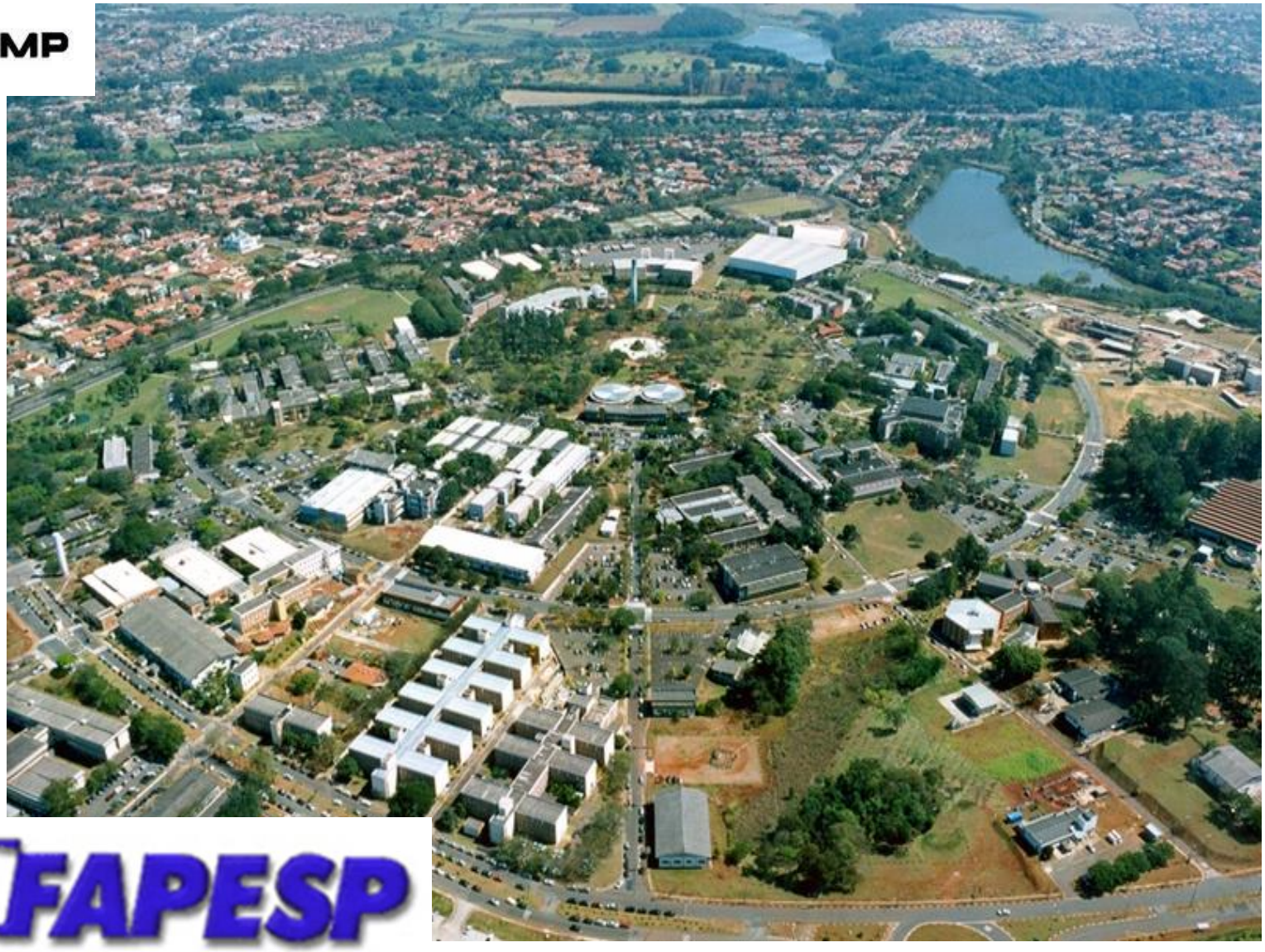

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