Bridging Gaps: Advancing Precision Medicine Implementation in Latin America's Diverse Genomic Landscape

Iscia Lopes-Cendes, M.D., Ph.D.

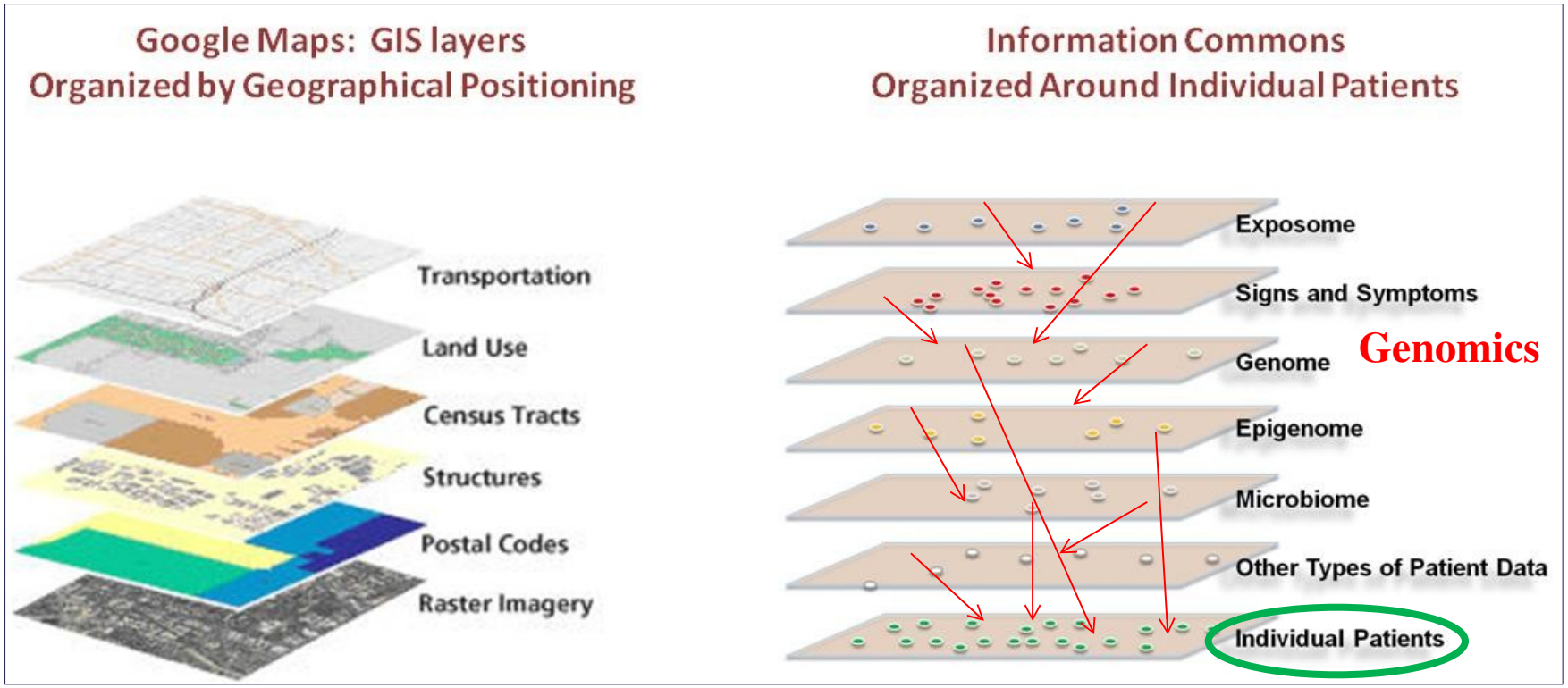
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Agenda

1. Role of genomics in precision medicine
2. Population genomics
3. The contribution of omics technologies for the study of disease mechanisms

Precision Medicine



Yamamoto et al. 2014

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nature genetics

Article https://doi.org/10.1038/s41588-023-01485-w

GWAS meta-analysis of over 29,000 people with epilepsy identifies 26 risk loci and subtype-specific genetic architecture

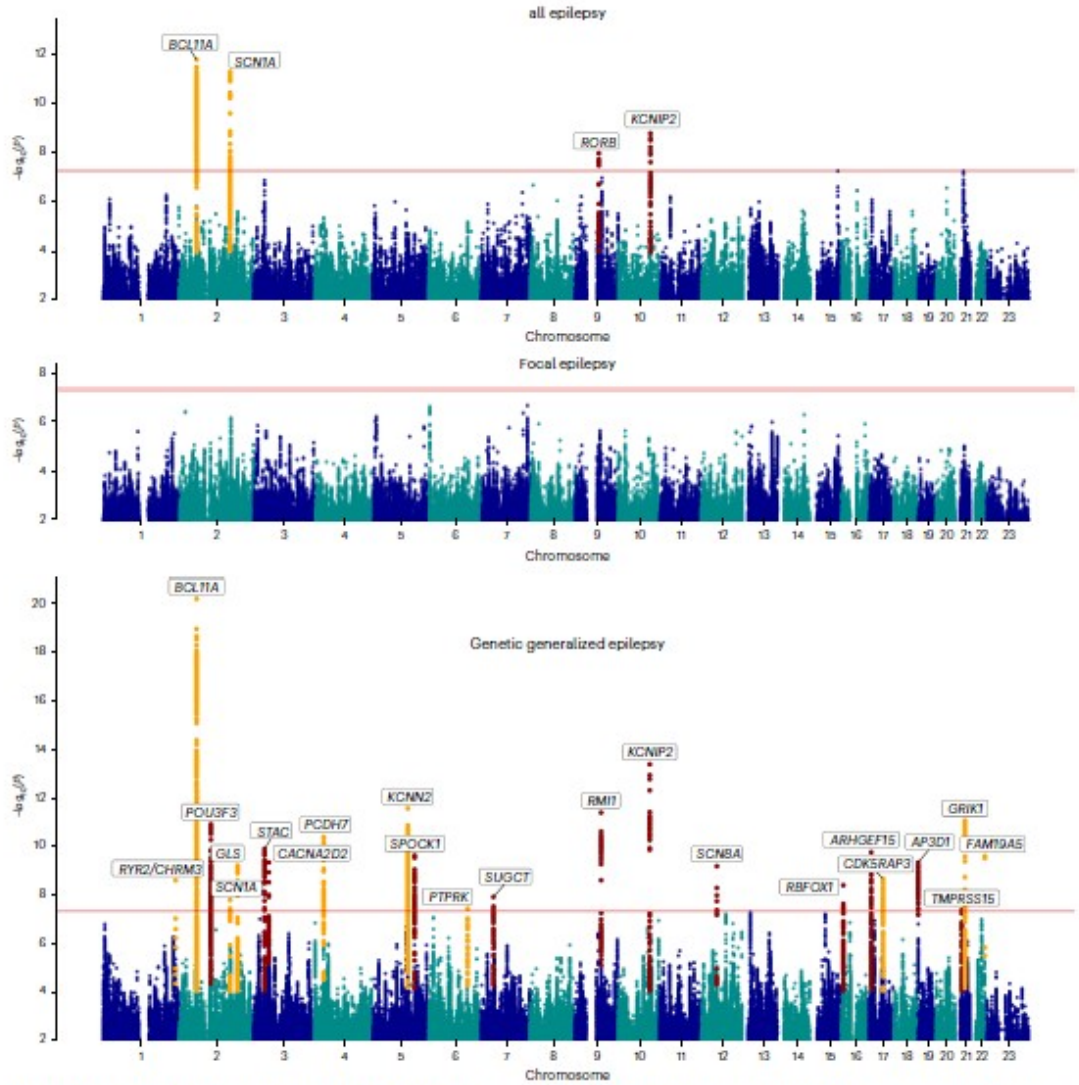
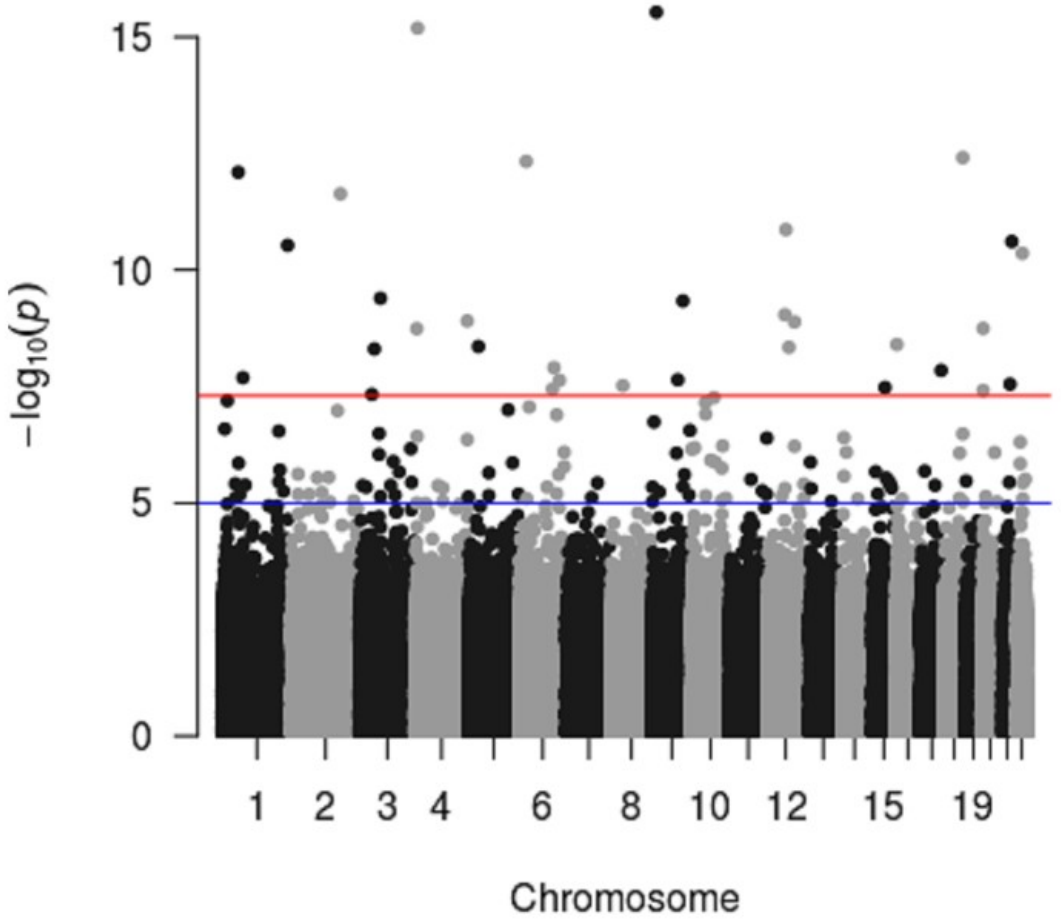
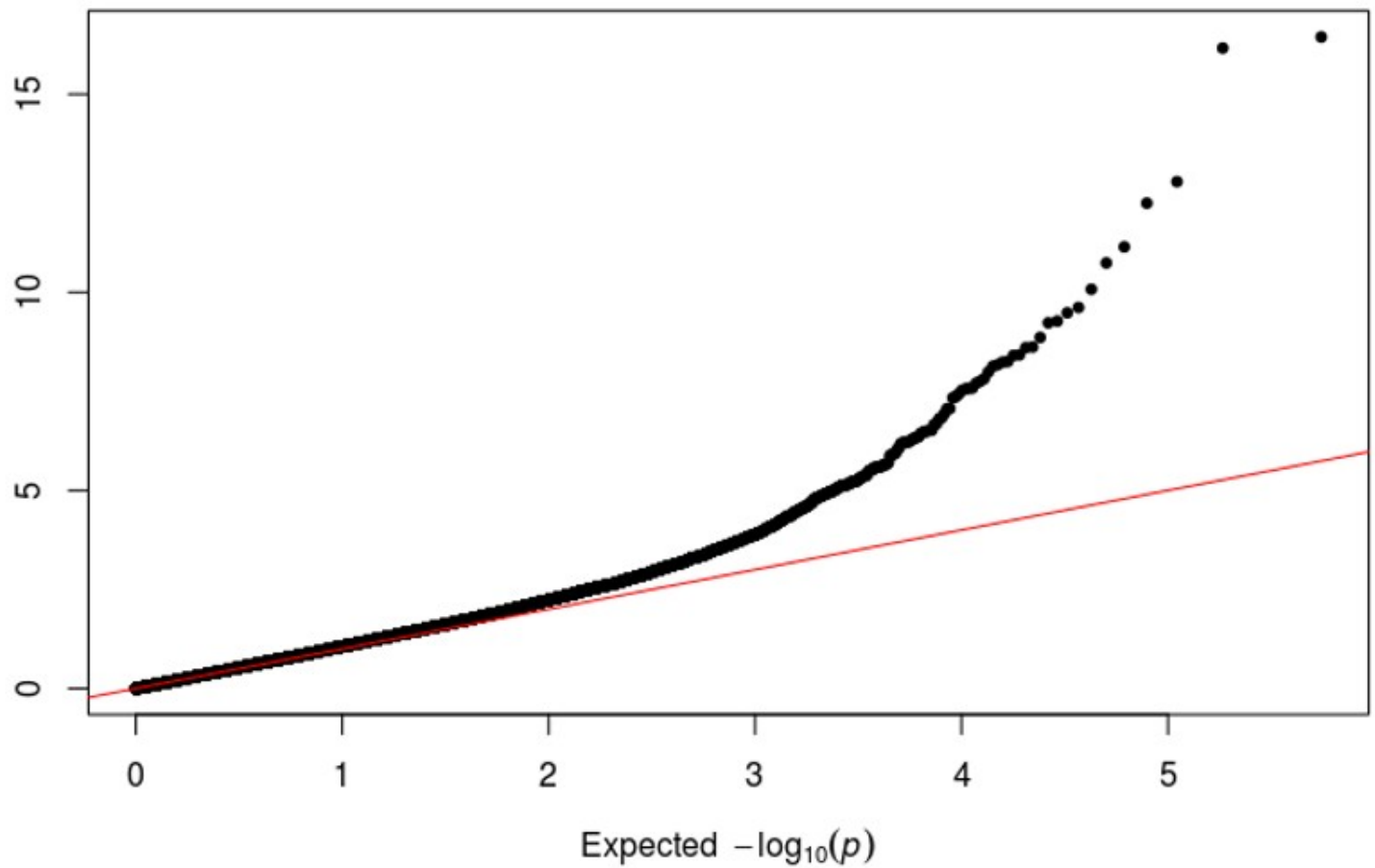


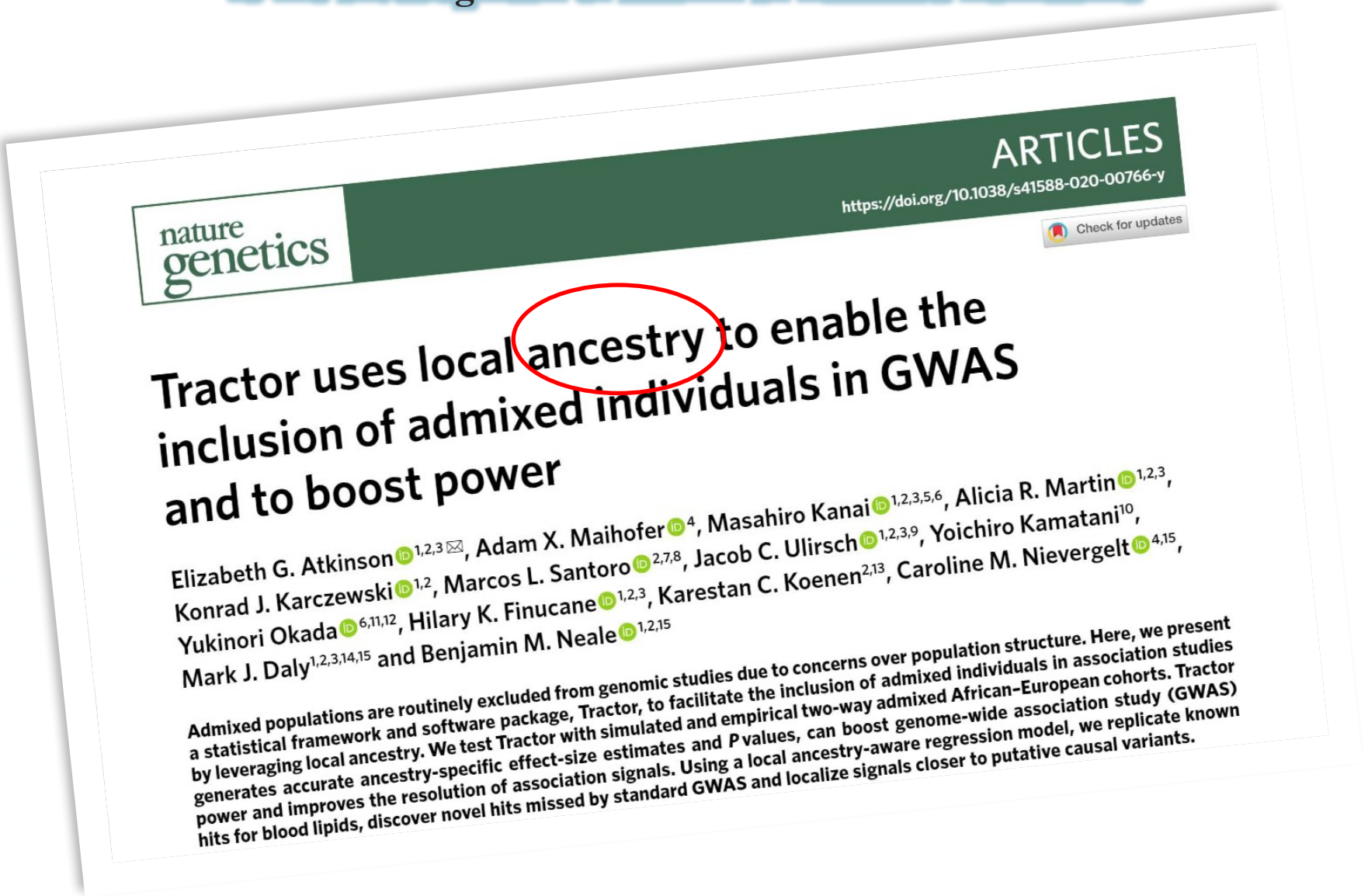
Fig. 1 | Manhattan plot of multi-ancestry all epilepsy (n = 29,944), focal epilepsy (n = 16,384) and genetic generalized epilepsy (n = 7,407) genome-wide meta-analyses, obtained by fixed-effects meta-analysis weighted by effective sample sizes. The red line shows the genome-wide significance threshold (5×10^{-8}). Chromosome and position are displayed on the x axis, and two-sided $-\log_{10}P$ value is on the y axis. New genome-wide significant loci are highlighted in red, and loci previously associated with epilepsy in orange. New loci were those previously unreported as GWAS significant in previous epilepsy GWASs. Annotated genes are those implicated by our gene prioritization analyses. See Supplementary Fig. 7 for QQ plots. QQ plots, quantile–quantile plot.

GWAS in Epilepsy (MTLE+HS)




15
10
5
0
0
1
2
3
4
5
Expected $-\log_{10}(p)$

Development of a protocol for genome-wide association study to be applied to the investigation of MTLE in admixed Brazilians



nature genetics

ARTICLES

https://doi.org/10.1038/s41588-020-00766-y

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Tractor uses local ancestry to enable the inclusion of admixed individuals in GWAS and to boost power

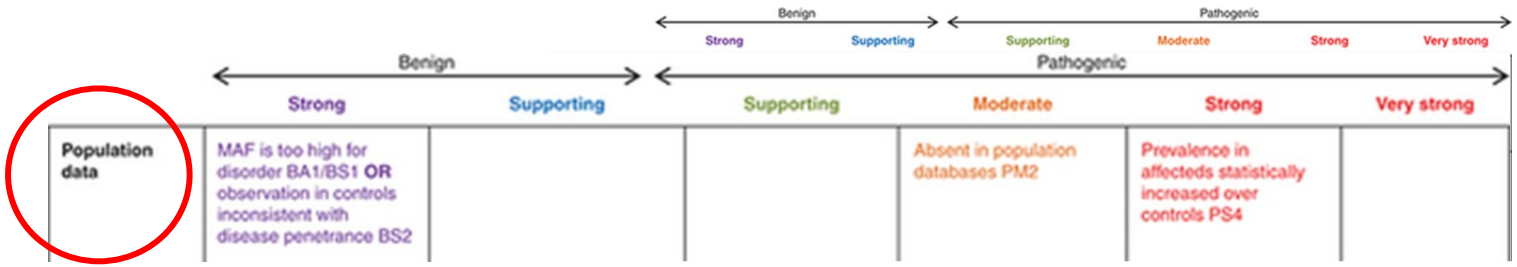
Elizabeth G. Atkinson[1,2,3]✉, Adam X. Maihofer[4], Masahiro Kanai[1,2,3,5,6], Alicia R. Martin[1,2,3], Konrad J. Karczewski[1,2], Marcos L. Santoro[2,7,8], Jacob C. Ulirsch[1,2,3,9], Yoichiro Kamatani[10], Yukinori Okada[6,11,12], Hilary K. Finucane[1,2,3], Karestan C. Koenen[2,13], Caroline M. Nievergelt[4,15], Mark J. Daly[1,2,3,14,15] and Benjamin M. Neale[1,2,15]

Admixed populations are routinely excluded from genomic studies due to concerns over population structure. Here, we present a statistical framework and software package, Tractor, to facilitate the inclusion of admixed individuals in association studies by leveraging local ancestry. We test Tractor with simulated and empirical two-way admixed African–European cohorts. Tractor generates accurate ancestry-specific effect-size estimates and *P* values, can boost genome-wide association study (GWAS) power and improves the resolution of association signals. Using a local ancestry-aware regression model, we replicate known hits for blood lipids, discover novel hits missed by standard GWAS and localize signals closer to putative causal variants.

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Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology

Sue Richards, PhD[1], Nazneen Aziz, PhD[2,16], Sherri Bale, PhD[3], David Bick, MD[4], Soma Das, PhD[5], Julie Gastier-Foster, PhD[6,7,8], Wayne W. Grody, MD, PhD[9,10,11], Madhuri Hegde, PhD[12], Elaine Lyon, PhD[13], Elaine Spector, PhD[14], Karl Voelkerding, MD[13] and Heidi L. Rehm, PhD[15]; on behalf of the ACMG Laboratory Quality Assurance Committee





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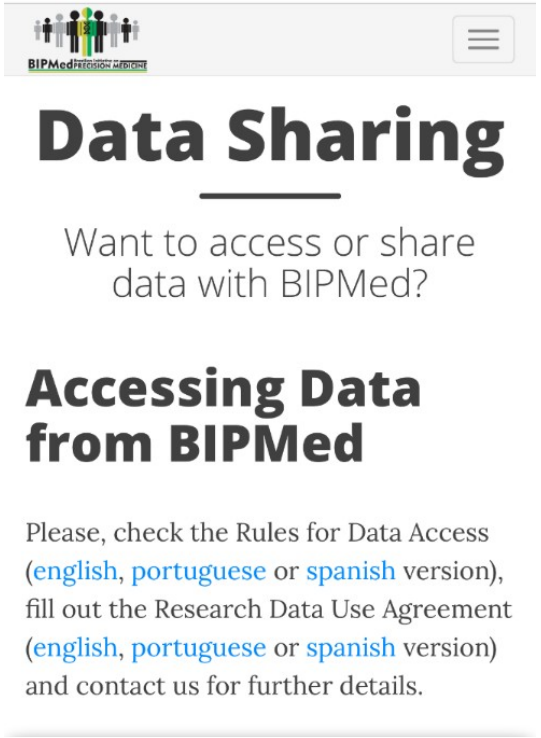
What do we do?

Databases

- Genomic Databases: BIPMed provides two databases containing pooled variant information of subjects from the Brazilian reference population (Campinas/SP region) and phenotype-specific databases:
    - BIPMed-WES-db provides information obtained from Whole Exome Sequencing experiments and includes 360 subjects;
    - BIPMed-Array-db contemplates 300 individuals and the data were obtained from microarray-based experiments (Affymetrix GenomeWide SNP 6.0 array).

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Data Sharing

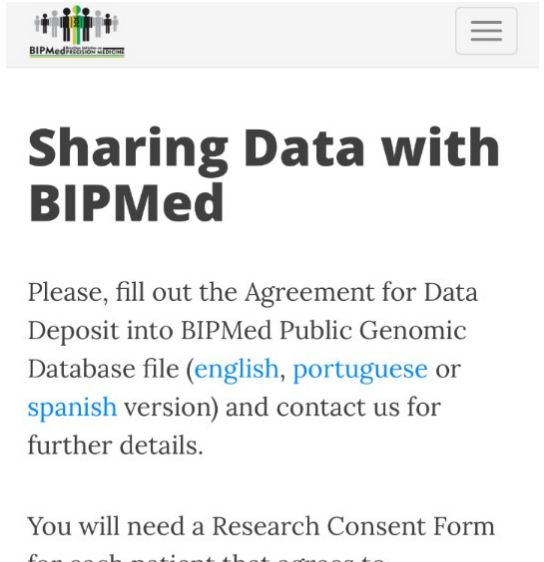


Data Sharing

Want to access or share data with BIPMed?

Accessing Data from BIPMed

Please, check the Rules for Data Access (english, portuguese or spanish version), fill out the Research Data Use Agreement (english, portuguese or spanish version) and contact us for further details.



Sharing Data with BIPMed

Please, fill out the Agreement for Data Deposit into BIPMed Public Genomic Database file (english, portuguese or spanish version) and contact us for further details.

You will need a Research Consent Form for each patient that agrees to participate in your project. Please, see a model of the Research Consent Form (english, portuguese or spanish version).

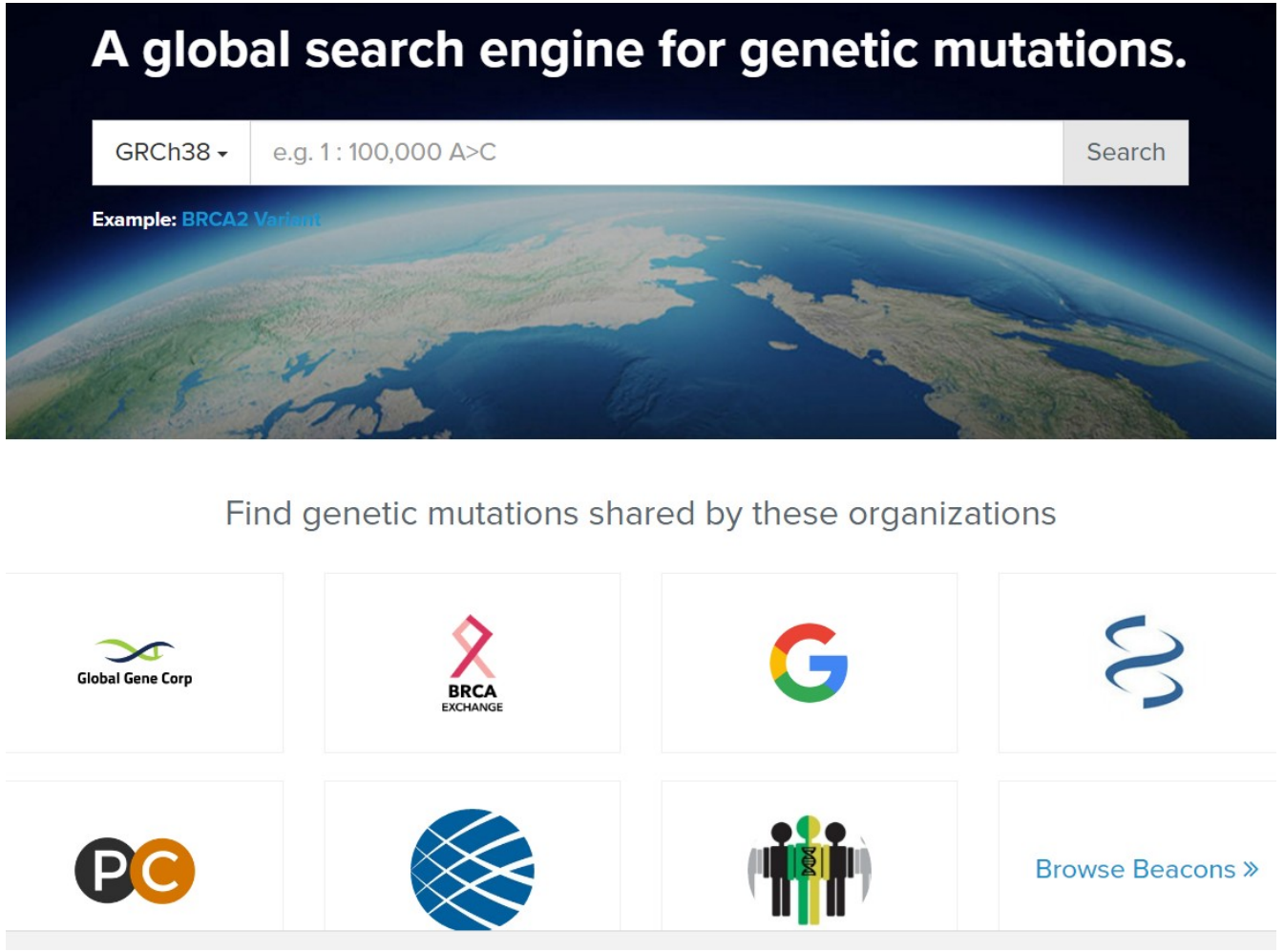
www.bipmed.org

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BEACON

Global Alliance for Genomics & Health

https://beacon-network.org



npj | Genomic Medicine

www.nature.com/npjgenmed

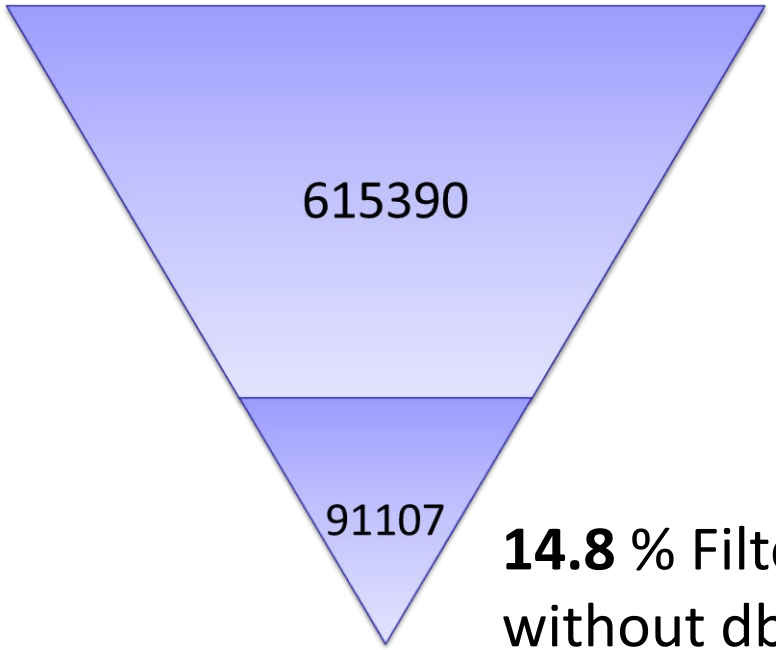
BRIEF COMMUNICATION OPEN

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The Brazilian Initiative on Precision Medicine (BIPMed): fostering genomic data-sharing of underrepresented populations

Cristiane S. Rocha[1,2,4], Rodrigo Secolin[1,2,4], Maíra R. Rodrigues[1,2], Benilton S. Carvalho[2,3] and Iscia Lopes-Cendes[1,2]✉

BIPMed-WES-db



14.8 % Filter variants without dbSNP ID

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Brazilian Initiative on Precision Medicine

Distribution of local ancestry and evidence of adaptation in admixed populations

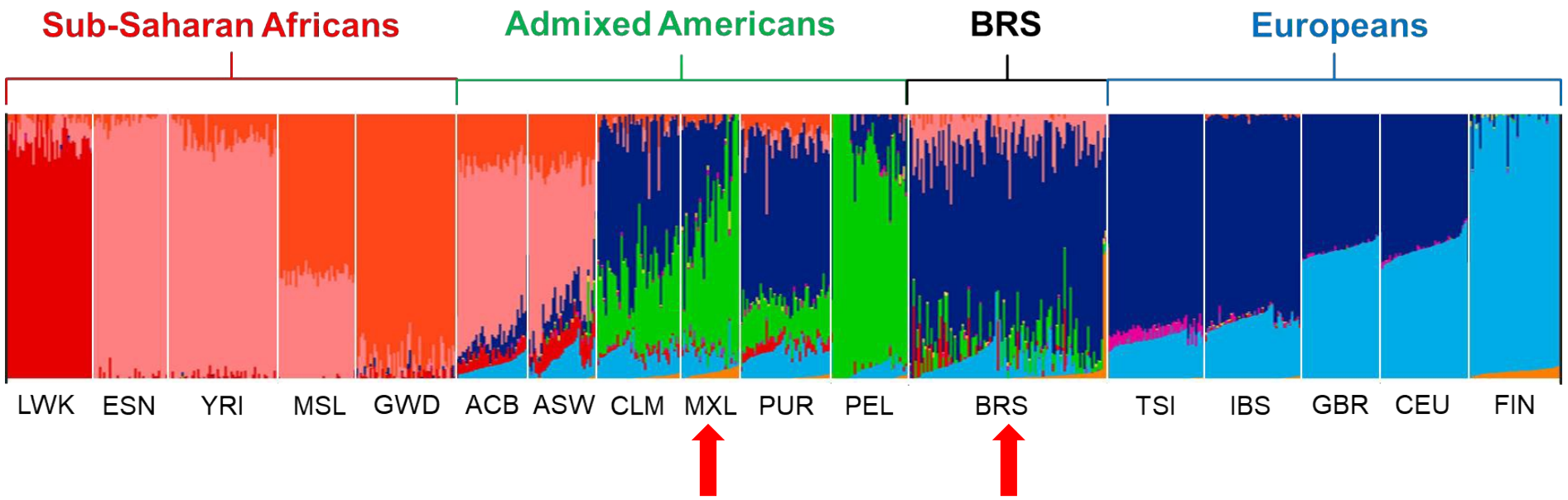
Rodrigo Secolin[1,2], Alex Mas-Sandoval[2,3], Lara R. Arauna[2], Fábio R. Torres[2], Tânia K. de Araujo[2], Maritza L. Santos[2], Cristiane S. Rocha[2], Benilton S. Carvalho[4], Fernando Cendes[3], Iscia Lopes-Cendes[3] & David Comas[2]

www.nature.com/scientificreports

SCIENTIFIC REPORTS
nature research

Global ancestry inference

- Admixture algorithm: best fit in K=10



Ancestry component	Mean proportion	Standard deviation
European	0.770	0.157
Sub-Saharan African	0.140	0.116
Native American	0.090	0.056

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Ananina G
2020

Fine scale genetic structure of the populations from three Brazilian regions

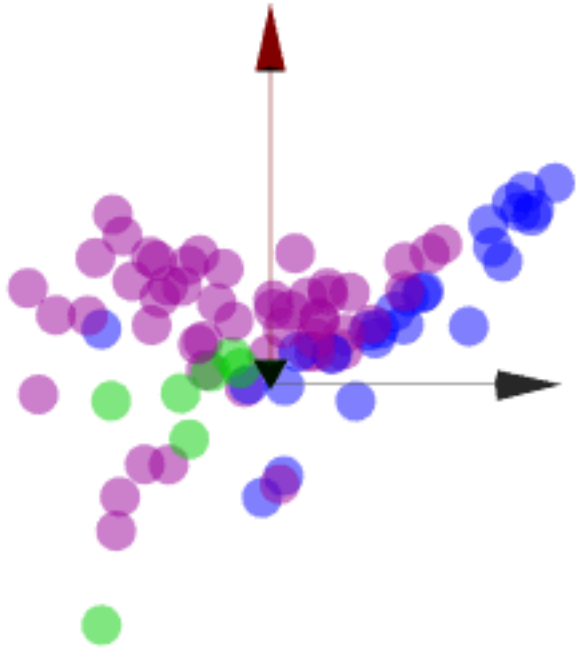
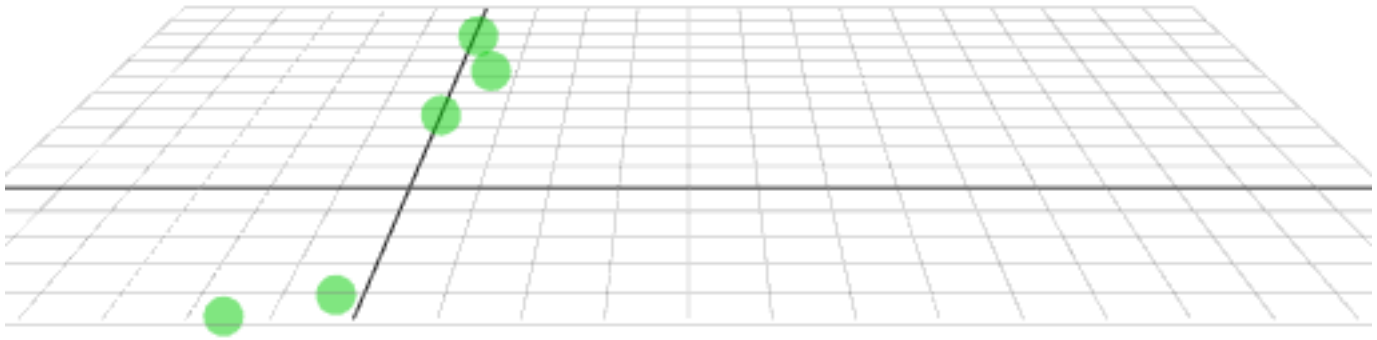


Gráfico de Componentes Principais: PC1 x PC2 x PC3

Recife, PE
Campinas, SP
Joinville,SP



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frontiers in Genetics

Exploring a Region on Chromosome 8p23.1 Displaying Positive Selection Signals in Brazilian Admixed Populations: Additional Insights Into Predisposition to Obesity and Related Disorders

Rodrigo Secolin[1], Marina C. Gonsales[2], Cristiane S. Rocha[2], Michel Naslavsky[2], Luiz De Marco[3], Maria A. C. Bicalho[4], Vinicius L. Vazquez[4], Mayana Zatz[2], Wilson A. Silva[5] and Iscia Lopes-Cendes[1]*

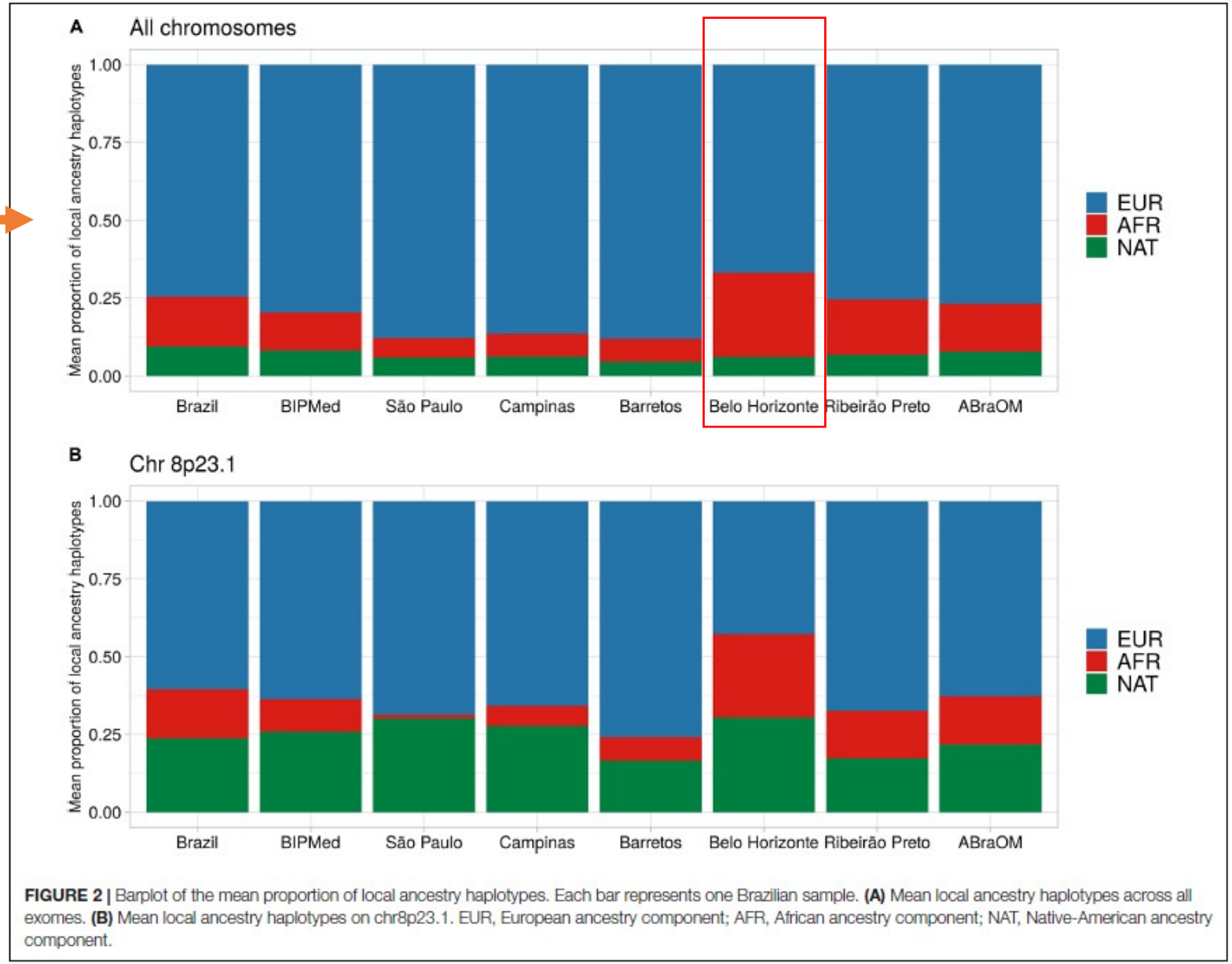


FIGURE 2 | Barplot of the mean proportion of local ancestry haplotypes. Each bar represents one Brazilian sample. **(A)** Mean local ancestry haplotypes across all exomes. **(B)** Mean local ancestry haplotypes on chr8p23.1. EUR, European ancestry component; AFR, African ancestry component; NAT, Native-American ancestry component.

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Brazilian Initiative on Precision Medicine

frontiers | Frontiers in Genetics

TYPE Review
PUBLISHED 19 January 2023
DOI 10.3389/fgene.2023.1091269

A review of ancestrality and admixture in Latin America and the caribbean focusing on native American and African descendant populations

Thais C. De Oliveira[1,2], Rodrigo Secolin[1,2] and Iscia Lopes-Cendes[1,2]*

[1]Department of Translational Medicine, School of Medical Sciences, University of Campinas (UNICAMP), Campinas, Brazil, [2]The Brazilian Institute of Neuroscience and Neurotechnology (BRAINN), Campinas, Brazil

Journal of Community Genetics
https://doi.org/10.1007/s12687-024-00752-5

REVIEW

Check for updates

Population molecular genetics in Brazil: From genomic databases and research to the implementation of precision medicine

Thais C. de Oliveira[1,2] · Iscia Lopes-Cendes[1,2]

Received: 18 July 2024 / Accepted: 5 November 2024
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Abstract

Precision medicine (PM) stands on the brink of revolutionizing medical practice throughout the world, holding significant potential for enhancing patient outcomes. However, its practical implementation, particularly in resource-limited countries, is not without challenges. The success of PM largely hinges on the availability of extensive datasets, including genetic and genomic information. This paper delves into the PM landscape and the current state of genetic and genomic testing in Brazil. We also shed light on the unique challenges posed by the country's diverse population and discuss ongoing initiatives to tackle these obstacles.

Keywords Population genomics · Genomic medicine · Genetic testing · Genomics in Latin America

ANNUAL REVIEWS

Annual Review of Genomics and Human Genetics

Inequalities and Inclusion in Genomics Applied to Healthcare: A Latin American Perspective

Iscia Lopes-Cendes[1,2] and Thais C. de Oliveira[1,2]

[1]Department of Medical Genetics and Genomic Medicine, School of Medical Sciences, University of Campinas, Campinas, Brazil; email: icendes@unicamp.br, crippat@unicamp.br

[2]Brazilian Institute of Neuroscience and Neurotechnology, Campinas, Brazil

Annu. Rev. Genom. Hum. Genet. 2025. 26:2.1–2.6

The *Annual Review of Genomics and Human Genetics* is online at genom.annualreviews.org

https://doi.org/10.1146/annurev-genom-111224-100329

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The PPS model

www.nature.com/scientificreports

SCIENTIFIC REPORTS

OPEN

Received: 03 September 2015
Accepted: 15 February 2016
Published: 03 March 2016

RNA sequencing reveals region-specific molecular mechanisms associated with epileptogenesis in a model of classical hippocampal sclerosis

A. S. Vieira[1,†], A. H. de Matos[1,†], A. M. do Canto[1,†], C. S. Rocha[1,†], B. S. Carvalho[1,†], V. D. B. Pascoal[2,†], B. Norwood[3], S. Bauer[3], F. Rosenow[3], R. Gilioli[4], F. Cendes[5,†] & I. Lopes-Cendes[1]

www.nature.com/scientificreports

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nature research

OPEN

Laser microdissection-based microproteomics of the hippocampus of a rat epilepsy model reveals regional differences in protein abundances

Amanda M. do Canto[1,9], André S. Vieira[2,9], Alexandre H.B. Matos[1,9], Benilton S. Carvalho[3,9], Barbara Henning[1,9], Braxton A. Norwood[4,5], Sebastian Bauer[5,6], Felix Rosenow[5,6], Rovilson Gilioli[7], Fernando Cendes[8,9] & Iscia Lopes-Cendes[1,9*]

TYPE Original Research
PUBLISHED 15 March 2023
DOI 10.3389/fneur.2023.1023950

Transcriptome analyses of the cortex and white matter of focal cortical dysplasia type II: Insights into pathophysiology and tissue characterization

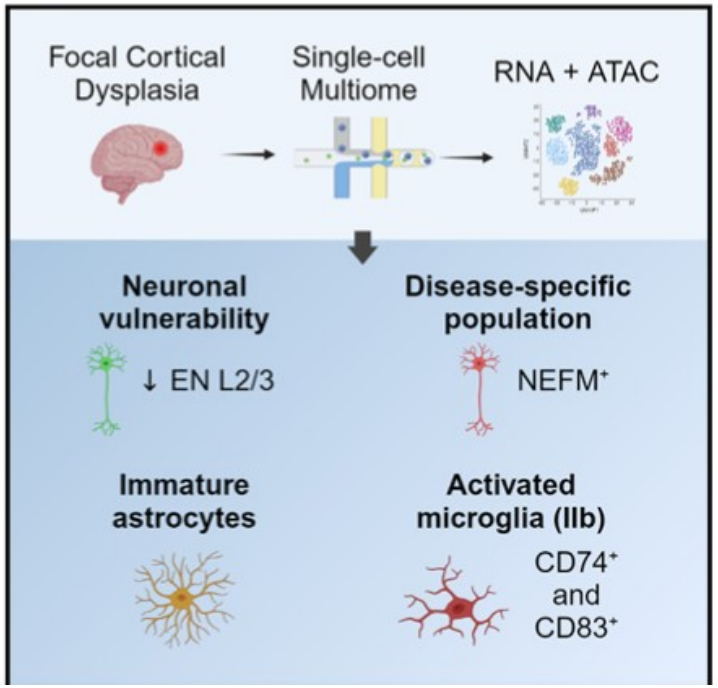
Guilherme Rossi Assis-Mendonça [1,2],
Maria Carolina Pedro Athié[2,3], João Vitor Gerdulli Tamanini[1,2],
Arethusa de Souza[1,2], Gabriel Gerardini Zanetti[2,4],
Patrícia Aline Oliveira Ribeiro de Aguiar Araújo[2,3],
Enrico Ghizoni[2,5], Helder Tedeschi[2,5],
Marina Koutsodontis Machado Alvim[2,5],
Vanessa Simão de Almeida[2,3], Welliton de Souza[2,3], Roland Coras[6],
Clarissa Lin Yasuda[2,5], Ingmar Blümcke[6],
André Schwambach Vieira[2,4], Fernando Cendes[2,5],
Iscia Lopes-Cendes[2,3] and Fabio Rogerio [1,2*]

iScience

Article

Multimodal single-cell profiling reveals neuronal vulnerability and pathological cell states in focal cortical dysplasia

Graphical abstract



Authors

Isabella C. Galvão, Manuela Lemoine, Lauana A. Messias, ..., Fabio Rogerio, Iscia Lopes-Cendes, Diogo F.T. Veiga

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In brief

Biological sciences; Neuroscience; Developmental neuroscience; Omics

Cold Spring Harbor Laboratory
bioRxiv
THE PREPRINT SERVER FOR BIOLOGY

Cell type mapping of mild malformations of cortical development with oligodendroglial hyperplasia in epilepsy using single-nucleus multiomics

Isabella C. Galvão, Manuela Lemoine, Ludmyla Kandratavicius, Clarissa L. Yasuda, Marina K. M. Alvim, Enrico Ghizoni, Ingmar Blümcke, Fernando Cendes, Fabio Rogerio, Iscia Lopes-Cendes, Diogo F. T. Veiga

bioRxiv 2024.12.12.628140; doi: https://doi.org/10.1101/2024.12.12.628140

https://doi.org/10.1093/brain/awab479 BRAIN 2022: 145; 1962–1977 | 1962

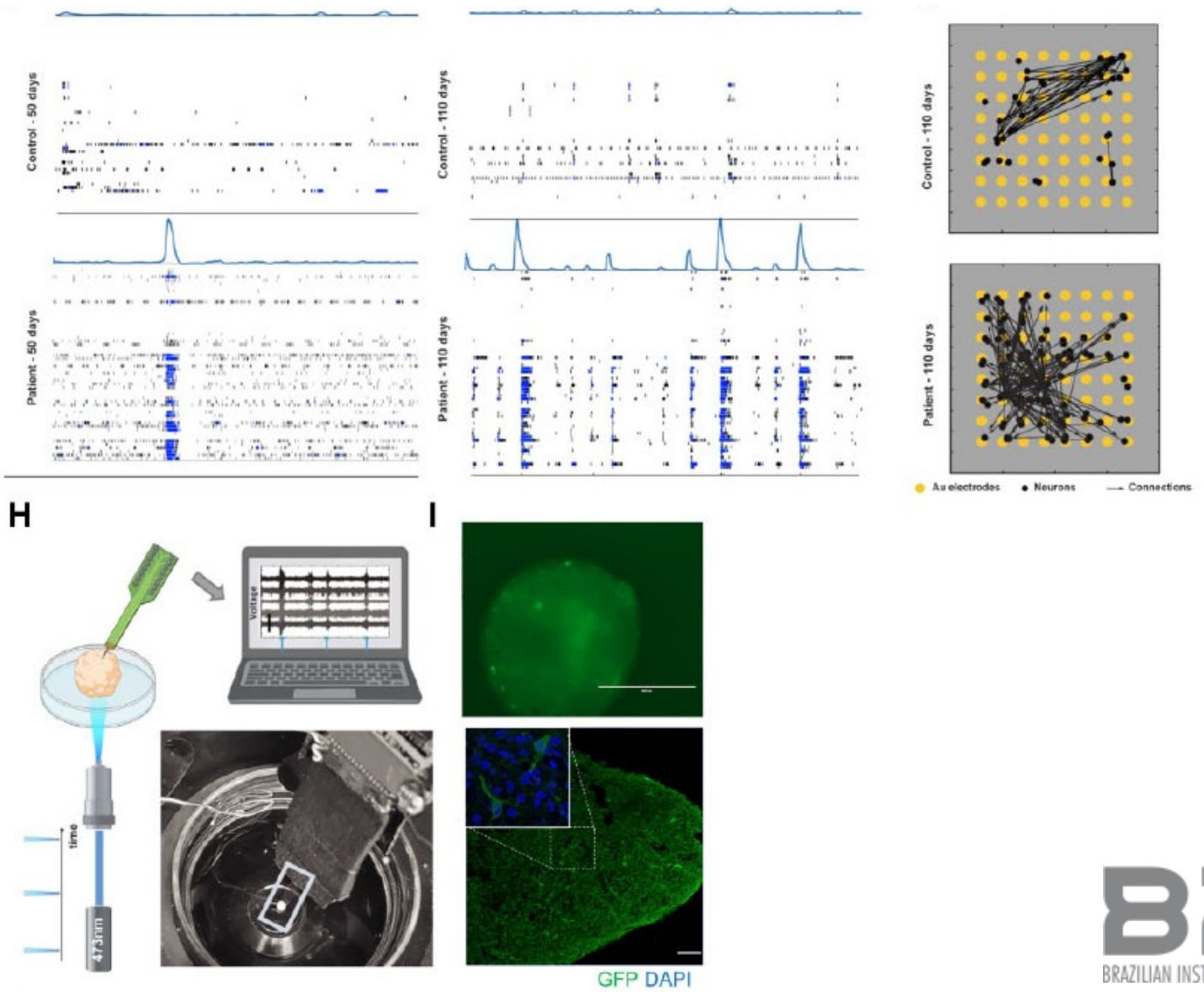
BRAIN
ORIGINAL ARTICLE

Junctional instability in neuroepithelium and network hyperexcitability in a focal cortical dysplasia human model

Simoni H. Avansini,[1,2,3] Francesca Puppo,[1] Jason W. Adams,[1] Andre S. Vieira,[3,4] Ana C. Coan,[3,5] Fabio Rogerio,[3,6] Fabio R. Torres,[2,3] Patricia A. O. R. Araújo,[2,3] Mariana Martin,[2,3] Maria A. Montenegro,[3,5] Clarissa L. Yasuda,[3,5] Helder Tedeschi,[3,5] Enrico Ghizoni,[3,5] Andréa F. E. C. França,[7] Marina K. M. Alvim,[3,5] Maria C. Athié,[2,3] Cristiane S. Rocha,[2,3] Vanessa S. Almeida,[2,3] Elayne V. Dias,[8] Lauriane Delay,[8] Elsa Molina,[9] Tony L. Yaksh,[8] Fernando Cendes,[3,5] Iscia Lopes Cendes[2,3] and Alysson R. Muotri[1,10]

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Control - 50 days
Patient - 50 days
Control - 110 days
Patient - 110 days
Control - 110 days
Patient - 110 days
Au electrodes
Neurons
Connections
H
I
voltage
time
473nm
GFP DAPI

Conclusions

- The implementation of PM in Brazil is in course, but additional population genomic studies are needed in underrepresented areas of the country
- Genomics and other omics technologies are important for PM: mechanism of disease, identify biomarkers and established improved disease models
- We have had productive collaborations with German investigators and are seeking new partnerships


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Course Directors:
Fabio Rogerio, Fernando Cendes & Ingmar Blümcke
For more information, please contact:
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- **Research Funds:**
  - **Fundação de Amparo a Pesquisa do Estado de São Paulo (FAPESP), BRAZIL**
  - **Conselho Nacional de Pesquisa (CNPq), BRAZIL**
  - **Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), BRAZIL**
  - **Chan-Zuckerberg Initiative (CZI)**







