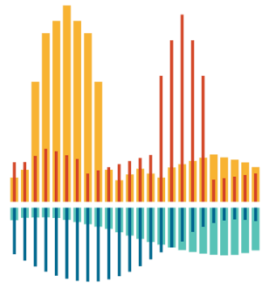


WHY BOTHER WITH DIVERSITY IN PRECISION MEDICINE RESEARCH?



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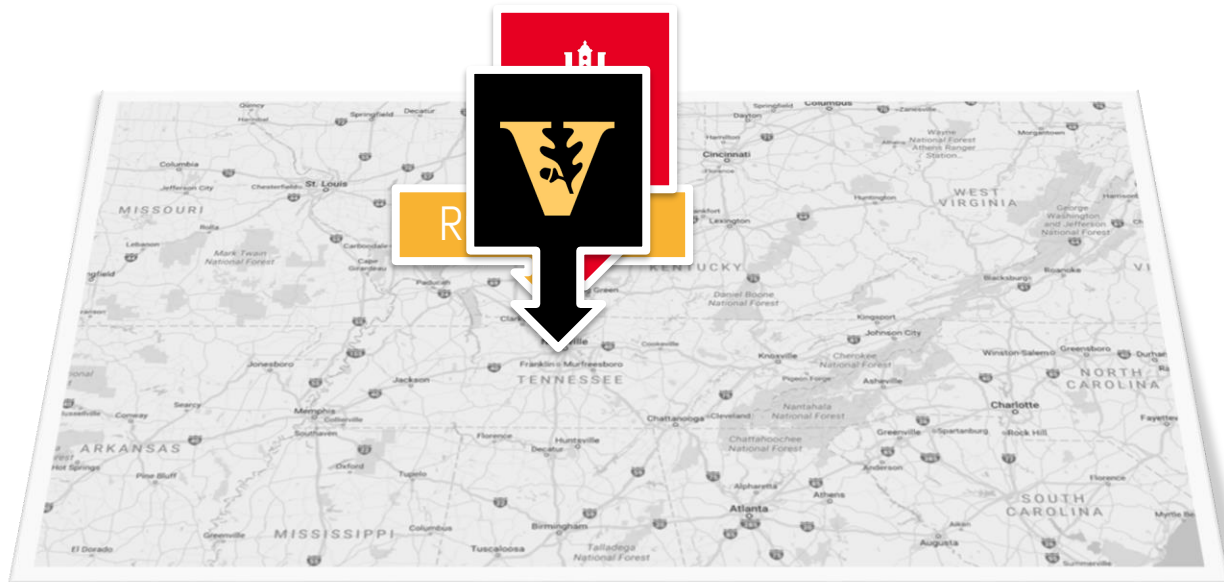
SCHOOL OF MEDICINE

CASE WESTERN RESERVE
UNIVERSITY

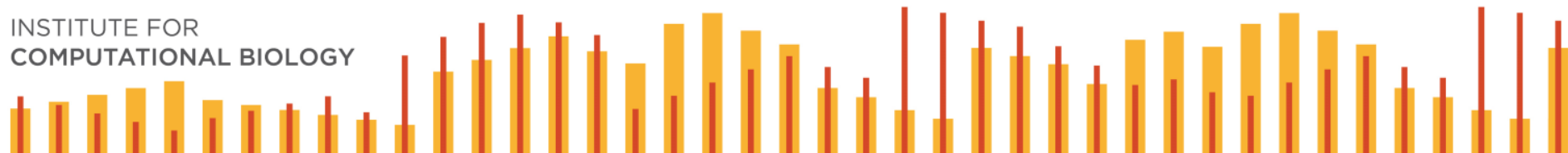
October 13, 2018

William S. Bush
Associate Professor
Institute for Computational Biology
Population and Quantitative Health Sciences

My Journey to GENOMICS AND PRECISION MEDICINE



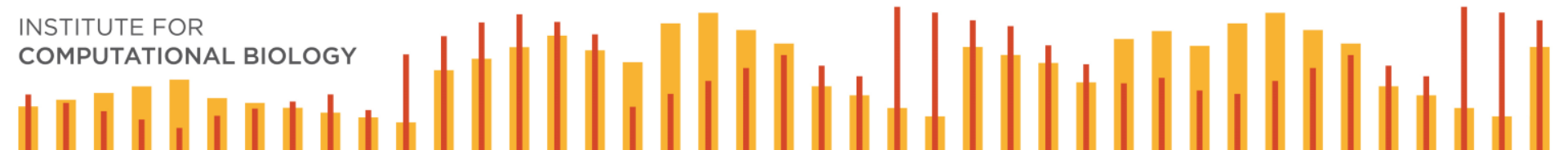
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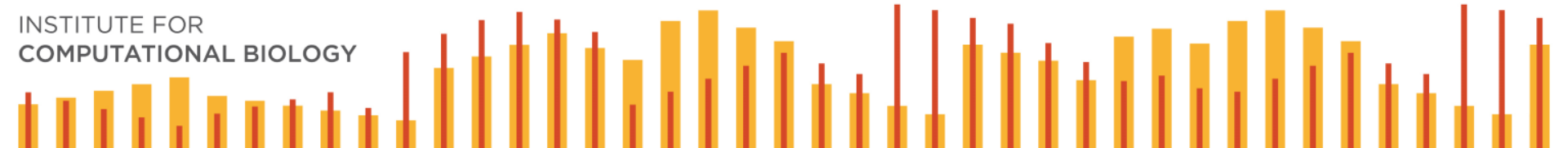
WHAT IS PRECISION MEDICINE?

Before giving you a medical treatment, we ideally want to know:

- Will this treatment be effective for you?
- What dose do you need?
- Are you at increased risk for side effects from this treatment?



INFINITE DIVERSITY IN INFINITE COMBINATIONS



TRAIT/PHENOTYPE

BEHAVIOR

ENVIRONMENT

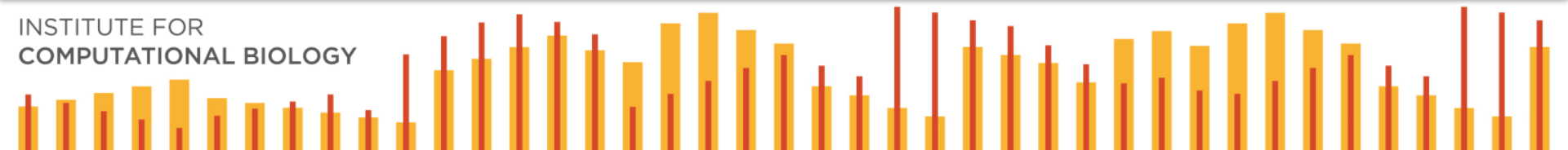
TISSUE/ORGAN FUNCTION

CELLULAR FUNCTION

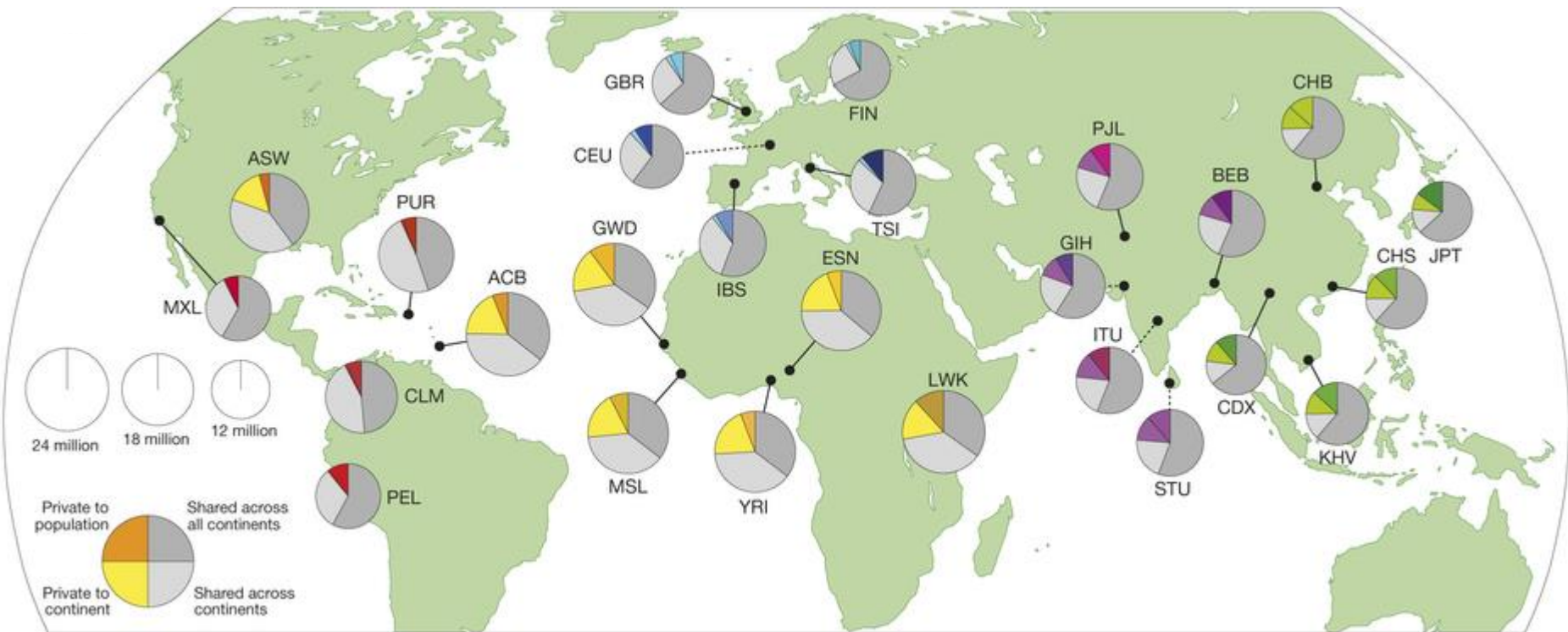
PROTEOME

TRANSCRIPTOME

GENOME



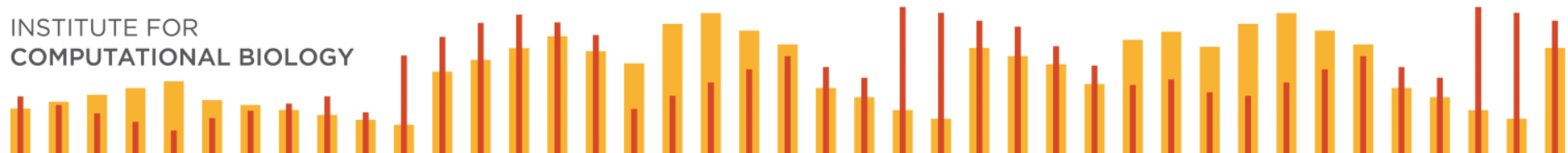
GENOMIC DIVERSITY OF HUMAN POPULATIONS



THE STATE OF GENOMIC DISCOVERY



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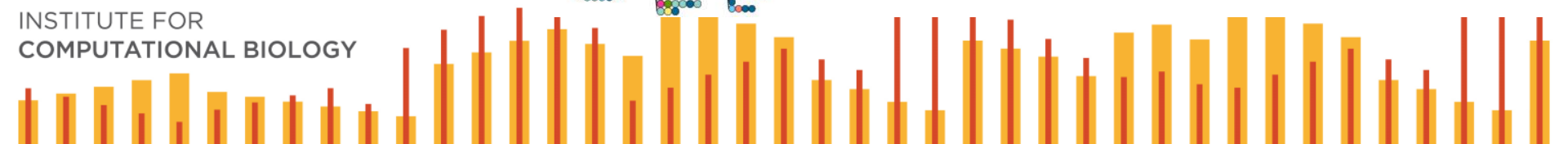
GWAS as of 9/30/2018:

3,596 publications

75,827

SNP-trait associations

<https://www.ebi.ac.uk/gwas/>

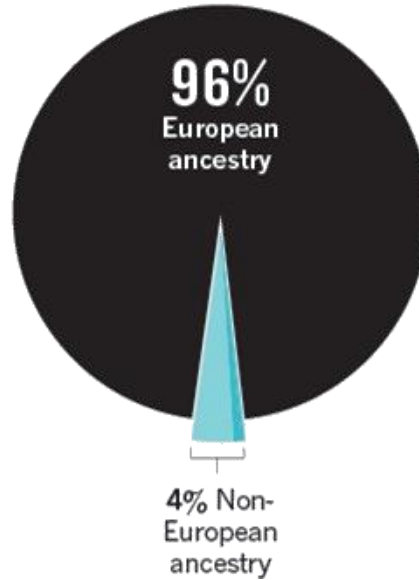


MOSTLY EUROPEAN-DESCENT

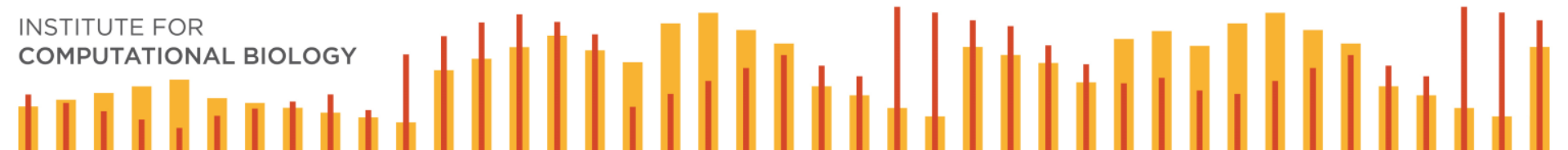
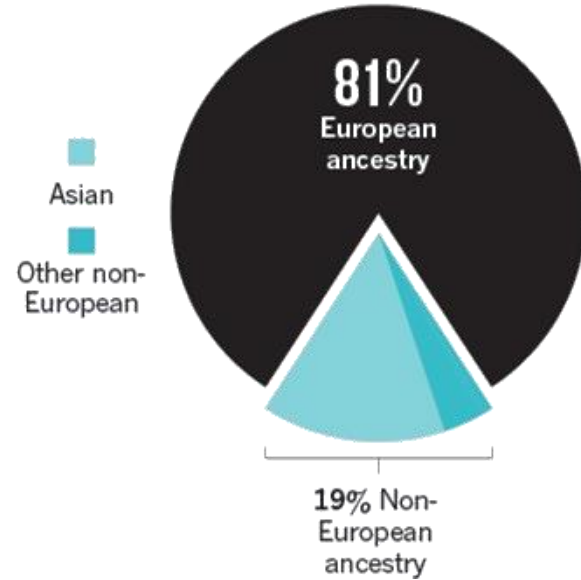
Bustamante, Burchard, de la Vega
(2011) *Nature* 475:163-165

Popejoy and Fullerton (2016)
Nature 538, 161–164

2009
373 studies
1.7 million samples



2016
2,511 studies
35 million samples



DIVERSITY IN RESEARCH MATTERS

SPECIAL ARTICLE

Genetic Misdiagnoses and the Potential for Health Disparities

Arjun K. Manrai, Ph.D., Birgit H. Funke, Ph.D., Heidi L. Rehm, Ph.D., Morten S. Olesen, Ph.D., Bradley A. Maron, M.D., Peter Szolovits, Ph.D., David M. Margulies, M.D., Joseph Loscalzo, M.D., Ph.D., and Isaac S. Kohane, M.D., Ph.D.

N Engl J Med 2016; 375:655-665 | August 18, 2016 | DOI: 10.1056/NEJMsa1507092

REPORT

Association of Trypanolytic ApoL1 Variants with Kidney Disease in African Americans

Giulio Genovese^{1,2,*}, David J. Friedman^{1,3,*}, Michael D. Ross⁴, Laurence Lecordier⁵, Pierrick Uzureau⁵, Barry I. Freedman⁶, Donald W. Bowden^{7,8}, Carl D. Langefeld^{8,9}, Taras K. Oleksyk¹⁰, Andrea L. Uscinski Knob⁴, Andrea J. Bernhardt¹, Pamela J. Hicks^{7,8}, George W. Nelson¹¹, Benoit Vanhollebeke⁵, Cheryl A. Winkler¹², Jeffrey B. Kopp¹¹, Etienne Pays^{5,†}, Martin R. Pollak^{1,13,†}

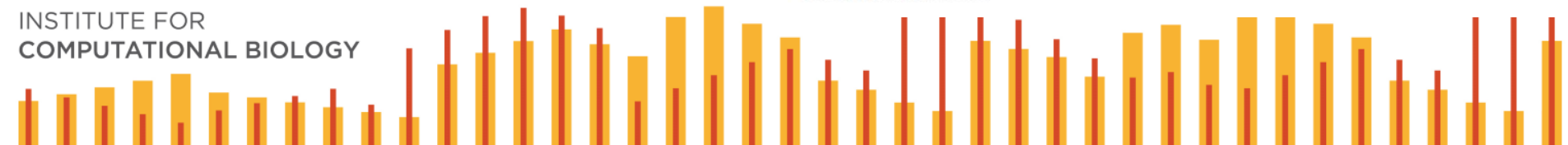
+ Author Affiliations

†To whom correspondence should be addressed. E-mail: mpollak@bidmc.harvard.edu (M.R.P.); epays@ulb.ac.be (E.P.)

‡* These authors contributed equally to this work.

Science 13 Aug 2010:
Vol. 329, Issue 5993, pp. 841-845
DOI: 10.1126/science.1193032

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PRECISION MEDICINE INITIATIVE COHORT PROGRAM

All of Us

Large

Linked to EHR

Oversample subgroups

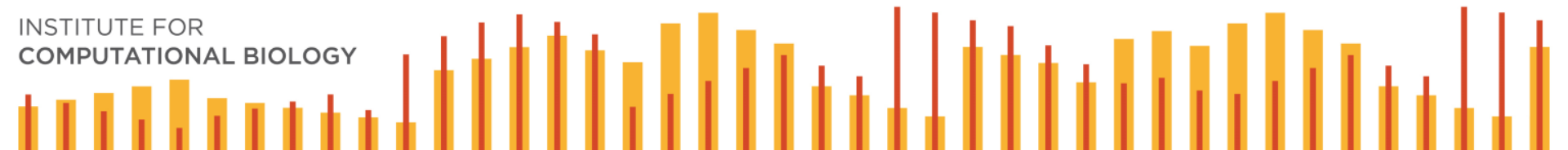
Re-contact for return of results

Wide age range

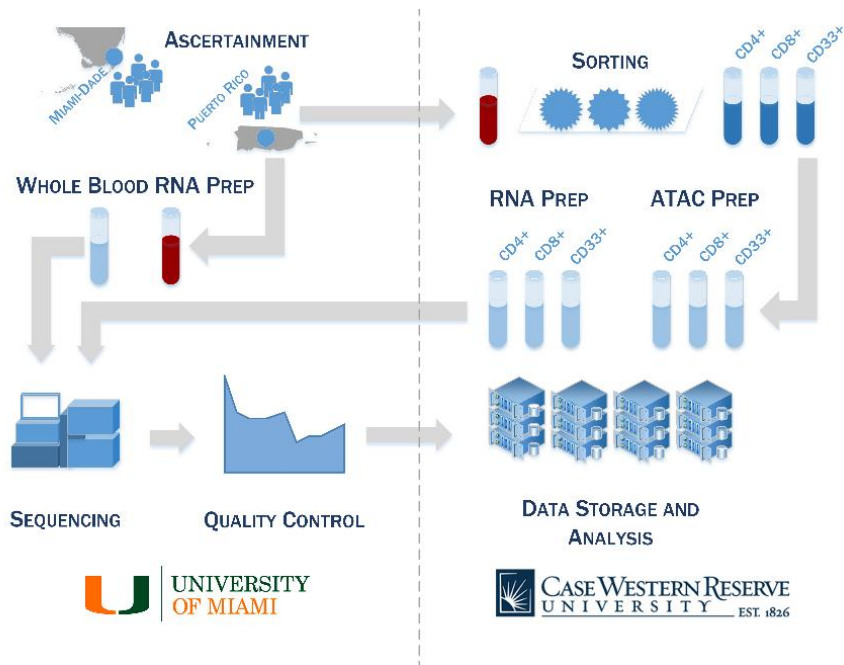
Lifestyle data collection

Rare & common disease

Extensive follow-up



MULTIPLE SCLEROSIS RISK IN PUERTO RICO

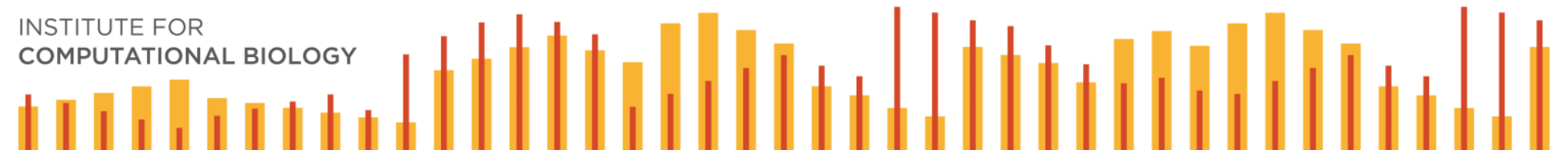


ARHMS

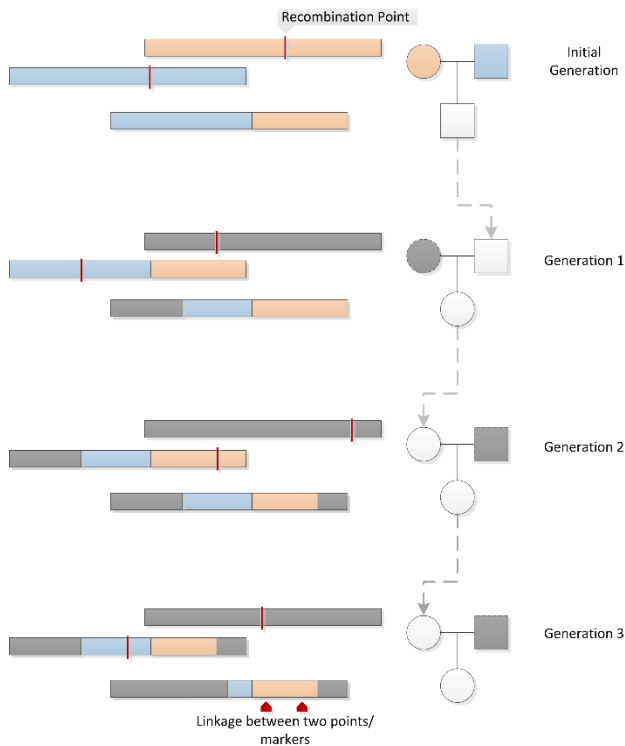
Alliance for Research
in Hispanic Multiple Sclerosis



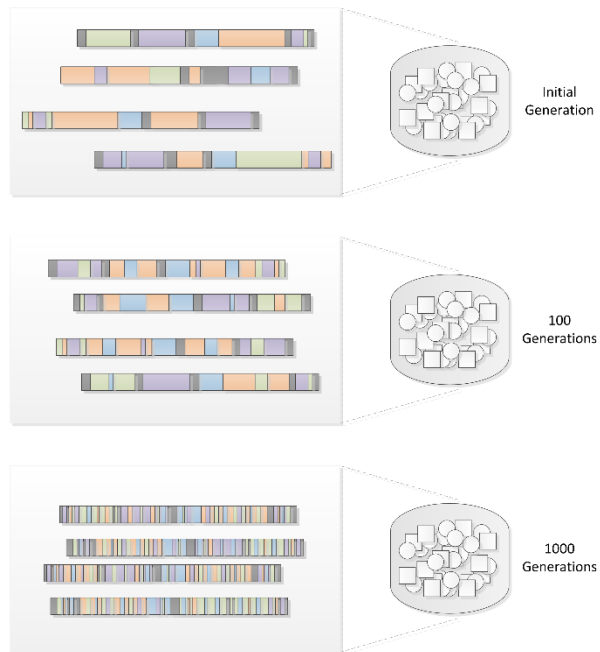
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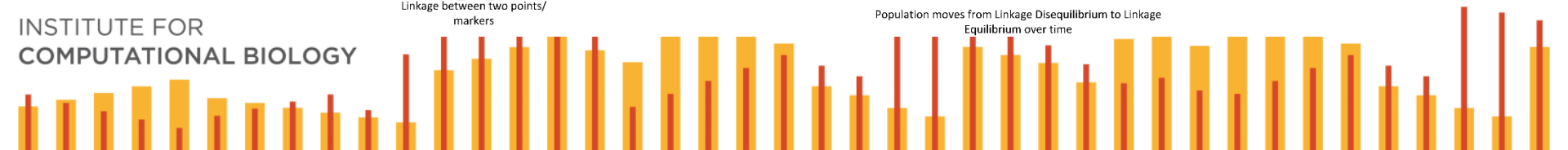
TRACING ANCESTRAL CHROMOSOMES



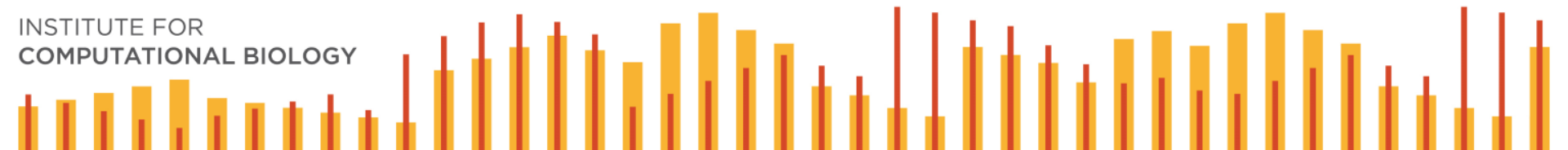
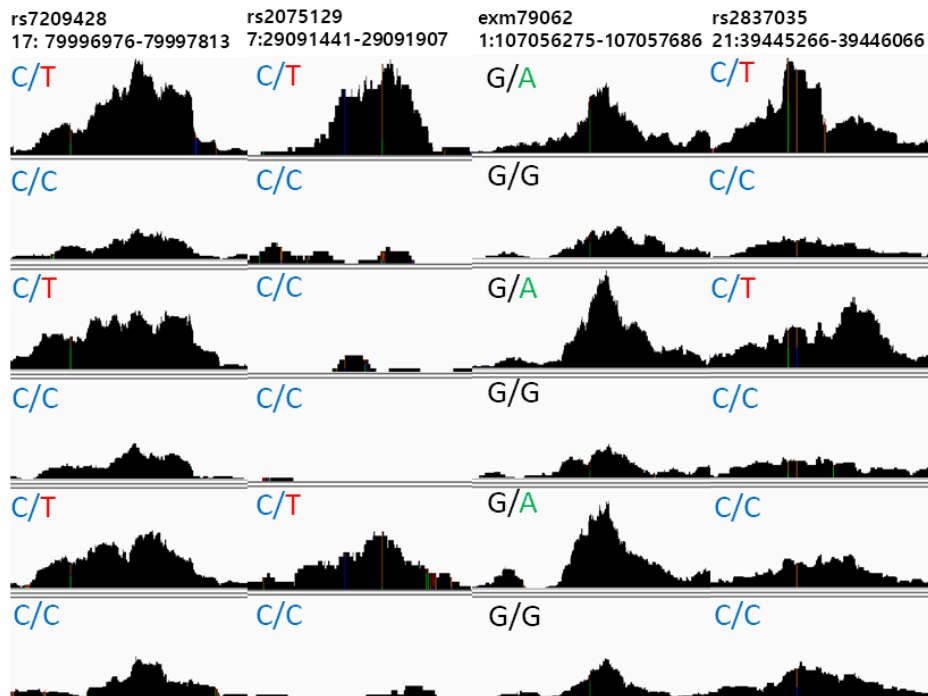
Decay of Linkage over successive generations



Population moves from Linkage Disequilibrium to Linkage Equilibrium over time

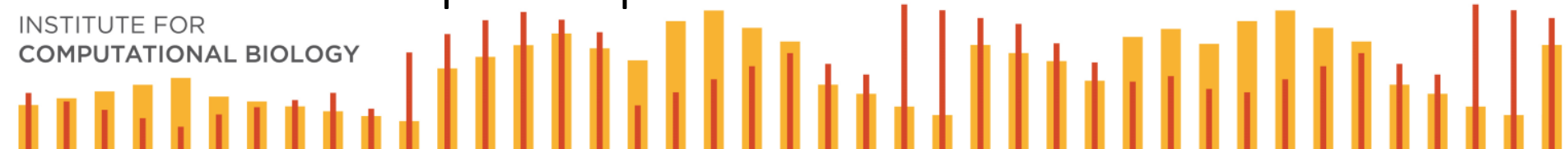


ATAC-SEQUENCING

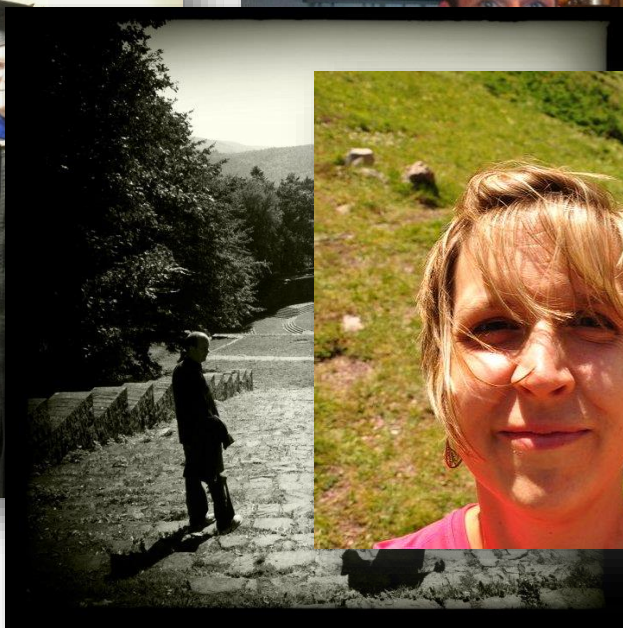
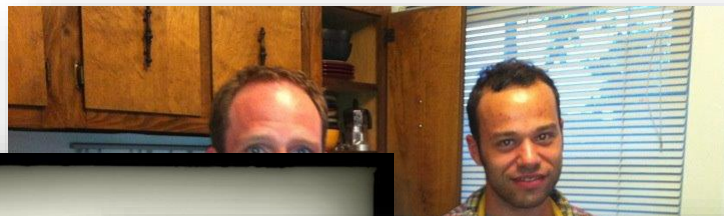


ADDING DIVERSITY TO STUDIES OF ALZHEIMER'S DISEASE

- Alzheimer's Disease Sequencing Project
- Whole genome sequence
- Addition of Dominican, Puerto Rican, and African American participants



WORKING WITH COOL PEOPLE



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