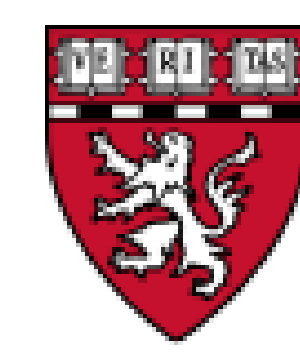




A customized genotype array to investigate the genetic architecture of tuberculosis in Peru

Y. Luo^{1,2}; L. Lecca³; R. Calderon³; C. Conteras³; R. Yataco³; Z.B. Zhang⁵; J. Galea³; B. Moody⁸; M. Murray^{3,4,5,6,7}; S. Raychaudhuri^{1,2}



HARVARD
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Background & Study design

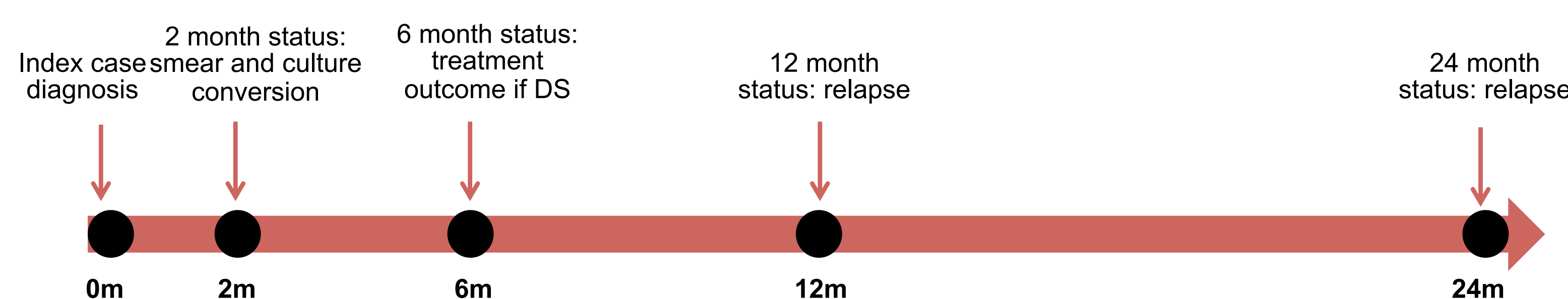
As a part of the Tuberculosis Research Unit program (TBRU) that aims to integrate basic and clinical research to study tuberculosis (TB) in countries where the disease is endemic, we are conducting

- the first genome-wide association study (GWAS) in a Latin Americana cohort in Lima, Peru
- a GWAS of **1,500** active TB cases and **1,500** *Mycobacterium tuberculosis* (*M.tb*) infected household contact controls
- first high phenotypic TB GWAS data

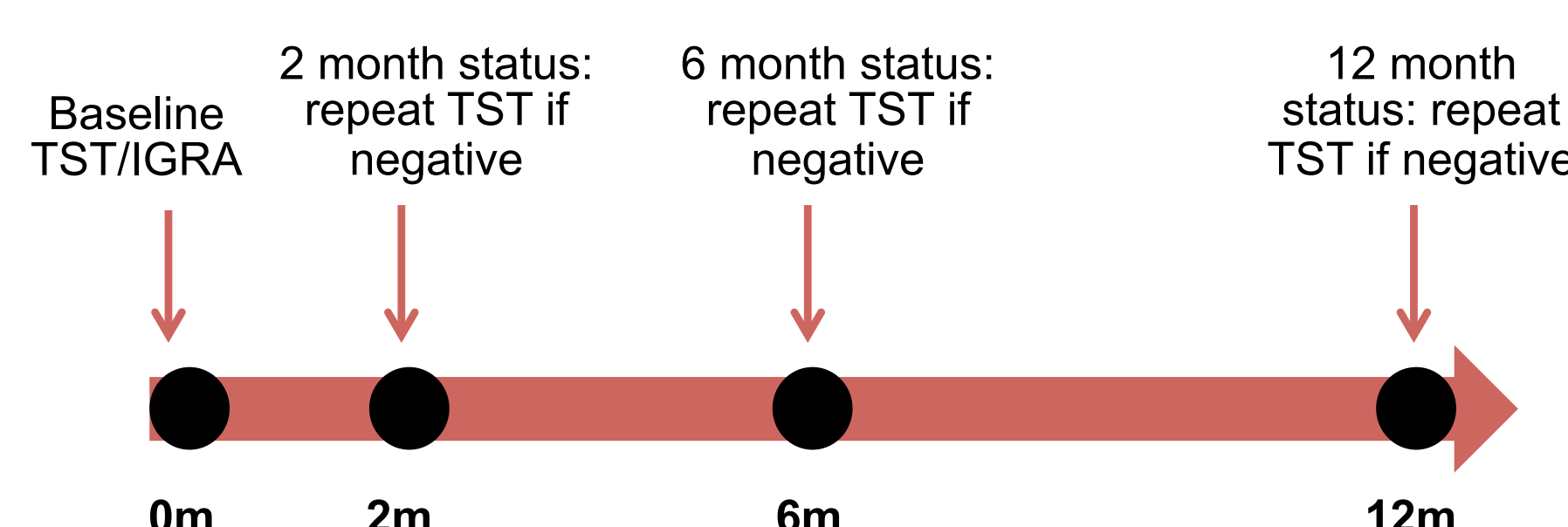
To further characterize variants specific to this group, especially those with tuberculosis, we initiated an exome sequencing pilot study of

- **116** patients with active TB
- cases without non-metabolic risk factors for TB (smoking, alcohol use, HIV) to enrich for possible genetic susceptibility to disease progression

Index cases



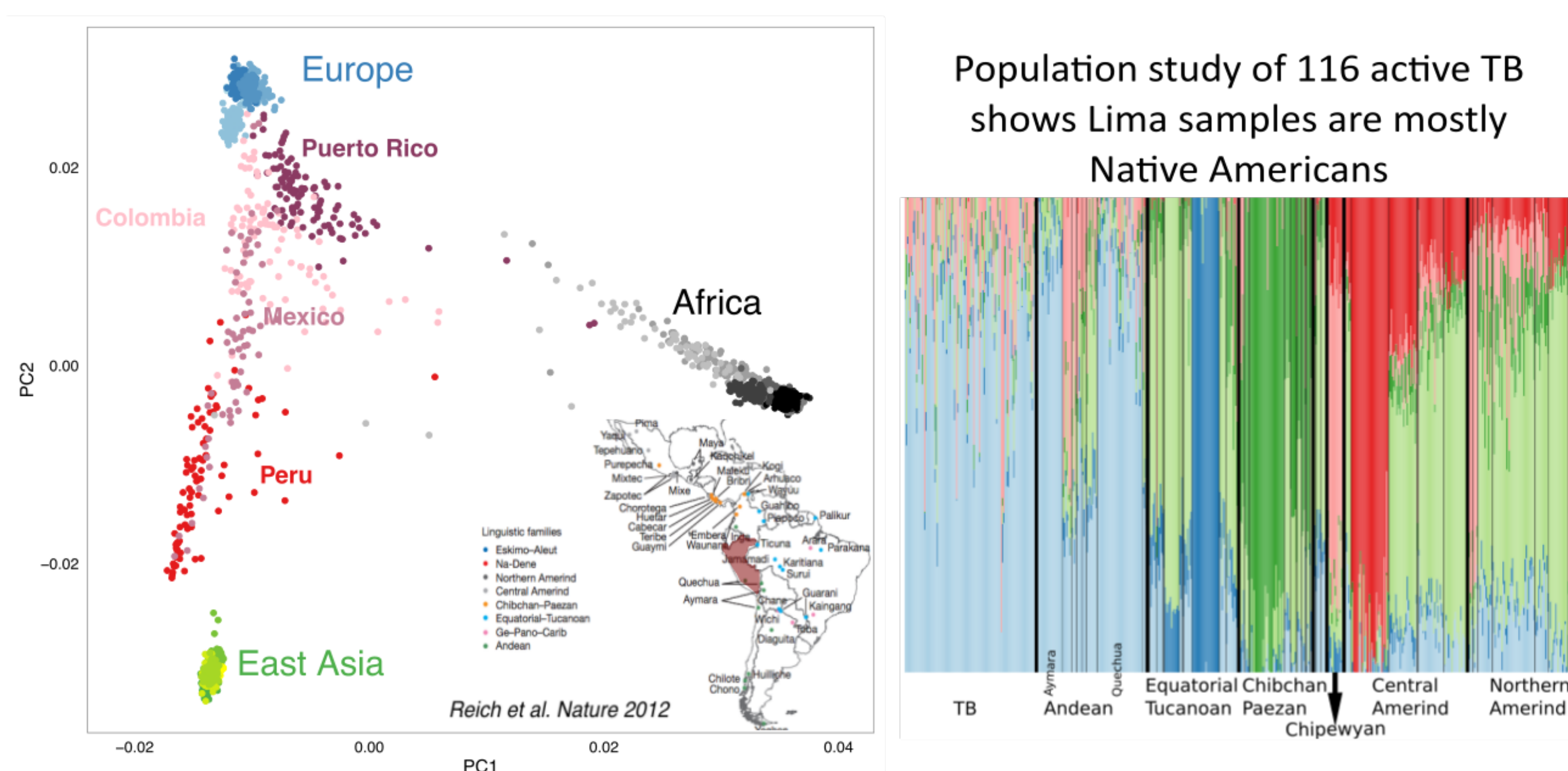
Household contacts



Index case outcomes:

- drug resistance status
- strain type
- treatment outcomes
- relapse

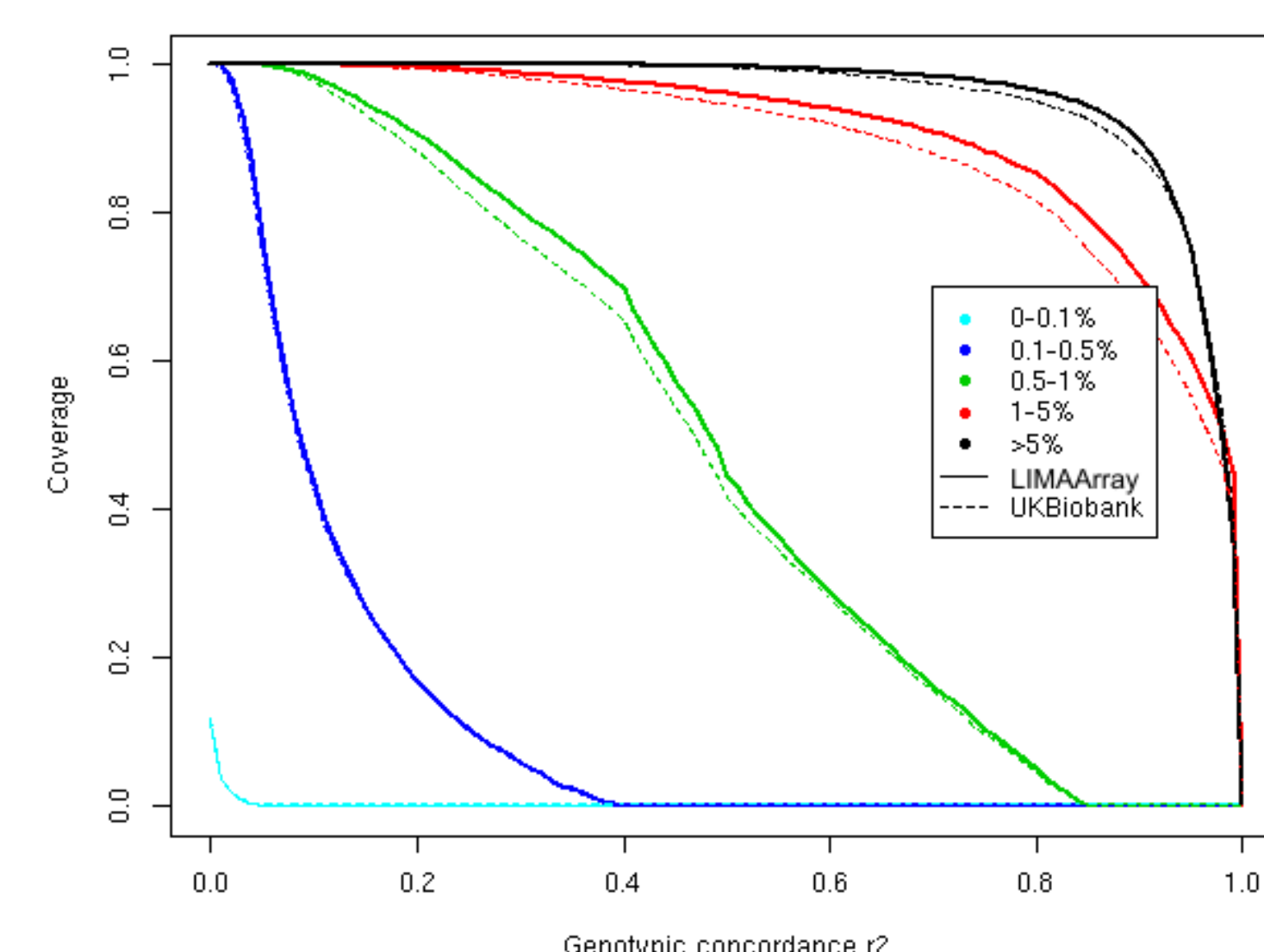
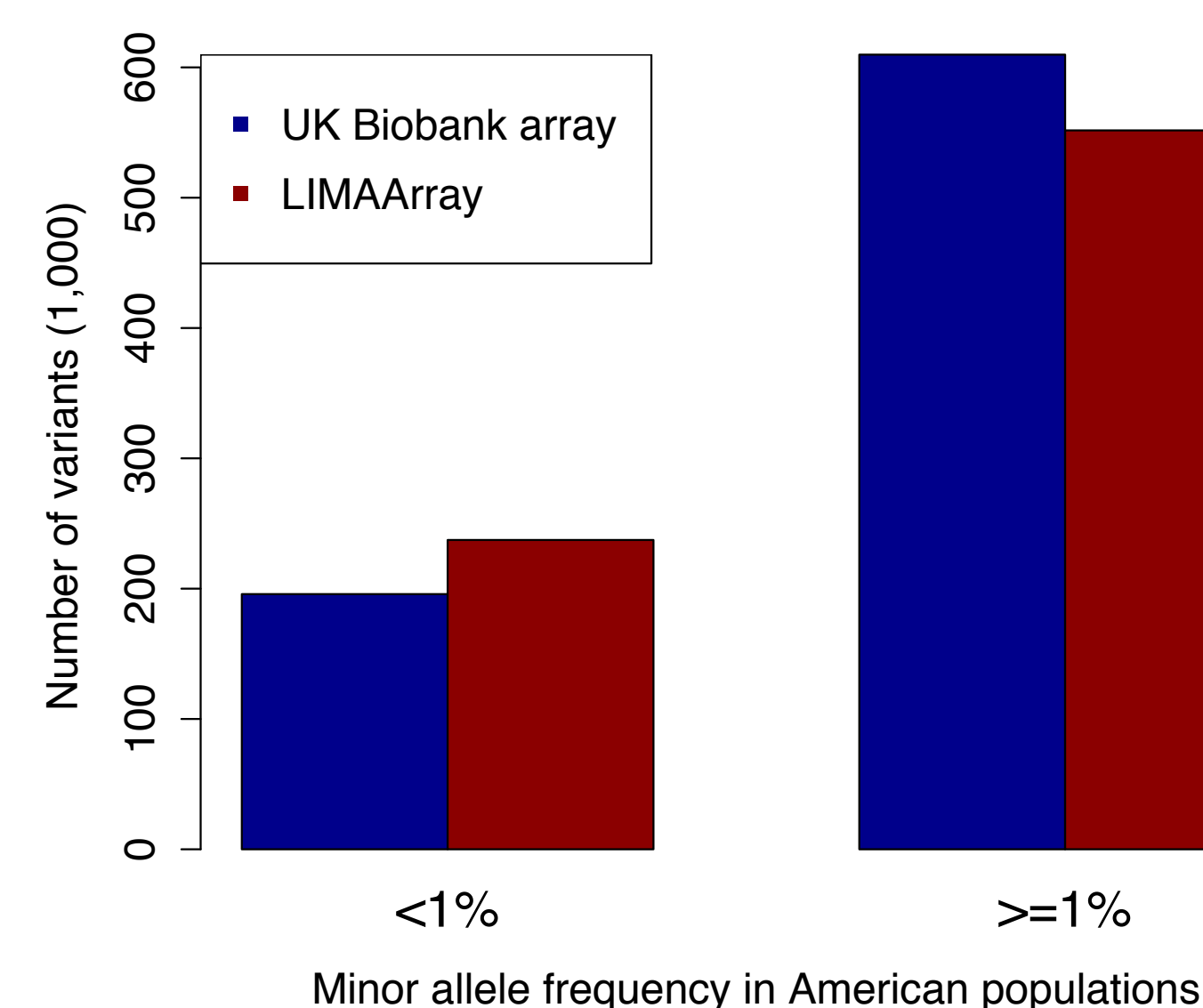
Unique genetic heritage of Peruvian population



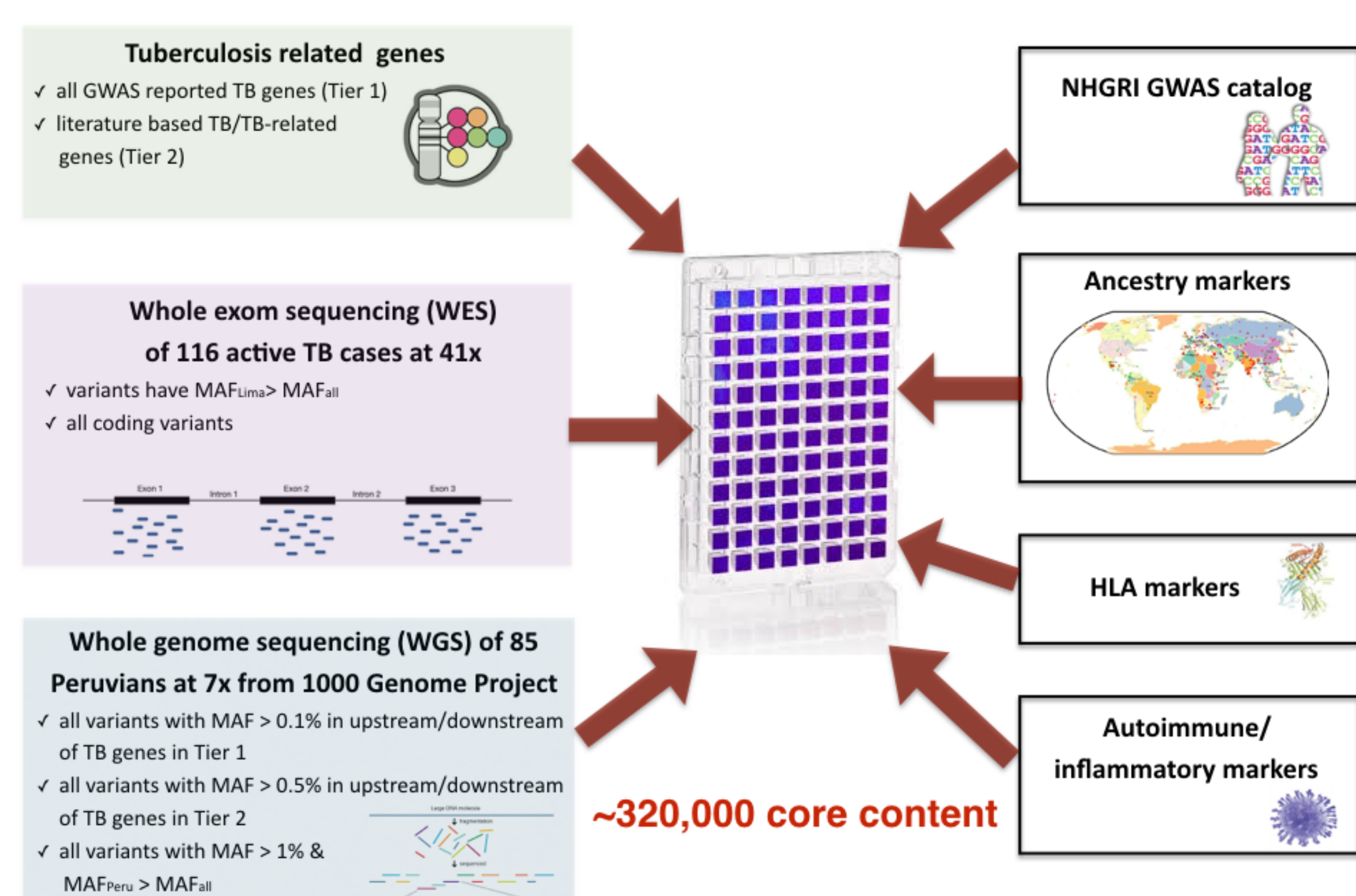
Evaluation

To evaluate the performance of *LIMAArray*, we

- imputed using 1000 Genomes Project Phase 3 reference panel
- cross-validated of **1/5** of Peruvian samples in 1000GP (10 runs)
- compared against *Axiom UK BioBank* genotype array
- calculated minor allele frequency in Peruvian population



LIMAArray Design



Summary and Ongoing work

- Identified unique genetic heritage of Peruvian population
- Designed a customized genotyping array tailored for Lima population, and demonstrated higher accuracy and coverage in Peruvian population in both common and rare variants
- First TB GWAS in Latin America
- First TB GWAS cohort has the ability to adjust for exposure differences
- Opportunities to investigate into relationships between TB and metabolic traits

Contact information

Yang Luo, PhD
E-mail: yangluo@broadinstitute.org
Twitter: [yluo86](https://twitter.com/yluo86)



¹Division of Genetics and Rheumatology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA.; ² Program in Medical and Population Genetics, Broad Institute of Harvard and MIT, Cambridge, MA, USA; ³ Socios En Salud, Lima, Peru; ⁴ Partners In Health, Boston, MA, USA; ⁵ Division of Global Health Equity, Brigham and Women's Hospital, Boston, MA, USA; ⁶ Department of Global Health and Social Medicine, Harvard Medical School, Boston, MA, USA; ⁷ Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA; ⁸ Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA