

The role of *Chlamydia trachomatis* genetic diversity in trachoma

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C. trachomatis and trachoma

- Contagious ocular infection caused by *Chlamydia trachomatis*

- Blinding eye disease
 - Chronic
 - Disabling

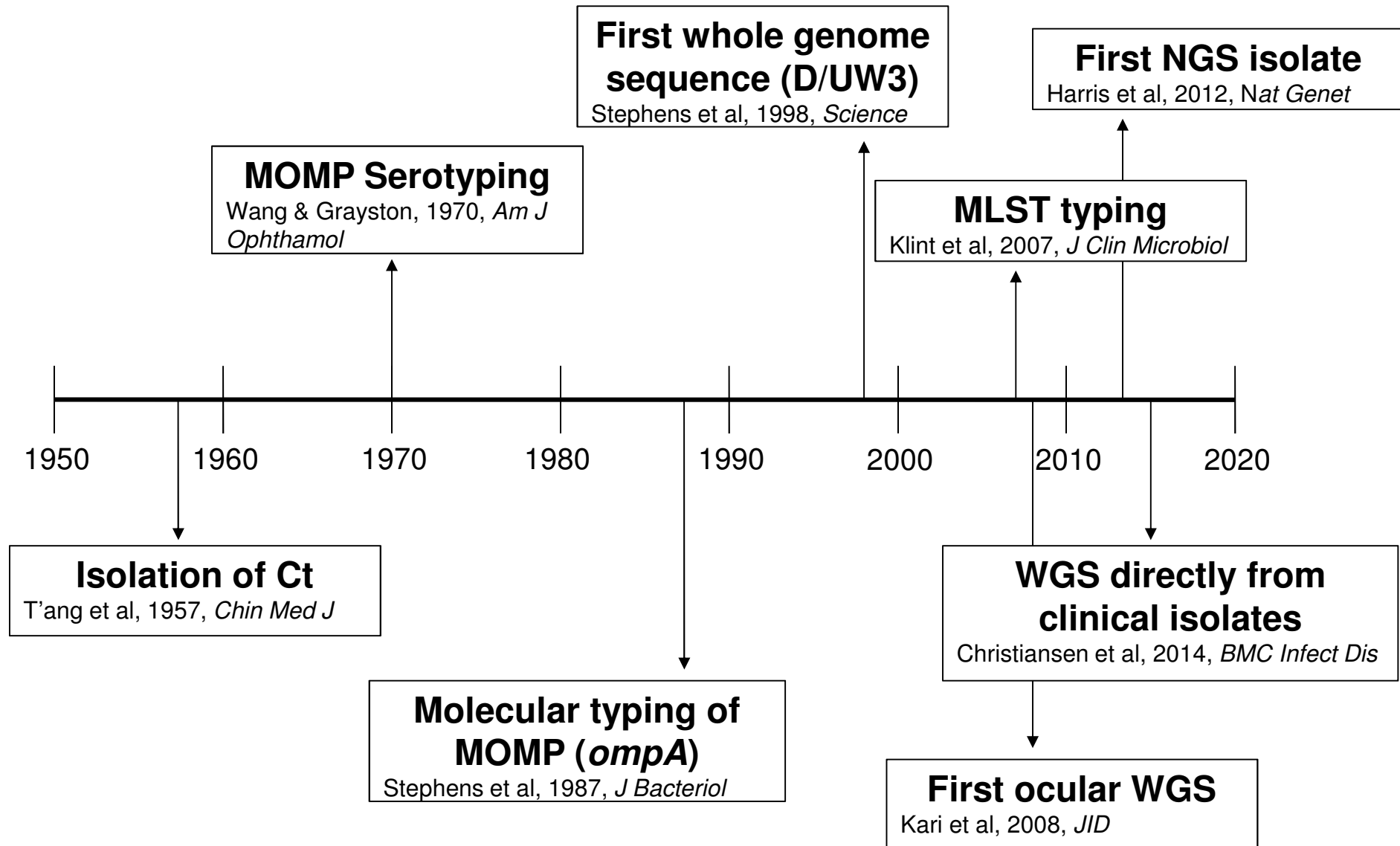


- Most common infectious cause of preventable blindness*
 - **>200 million** people live in trachoma endemic areas
 - 80% burden in 14 countries
 - **> 2 million** visually impaired
 - **3.2 million** require surgery to prevent blindness
 - **1.2 million** people are blind (3% global blindness)

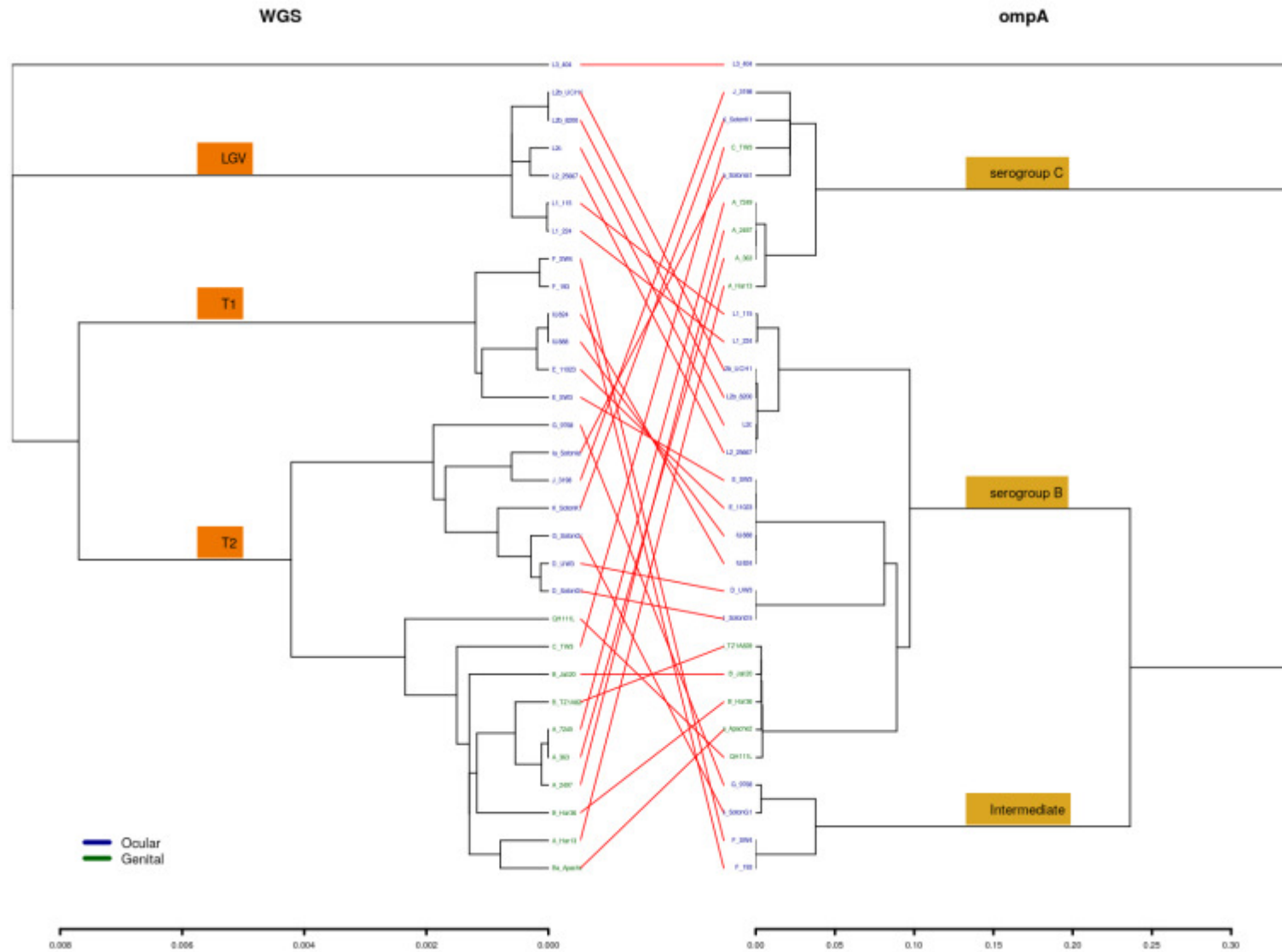
*WHO, 2016



History of Ct genomics



Ct typing methods



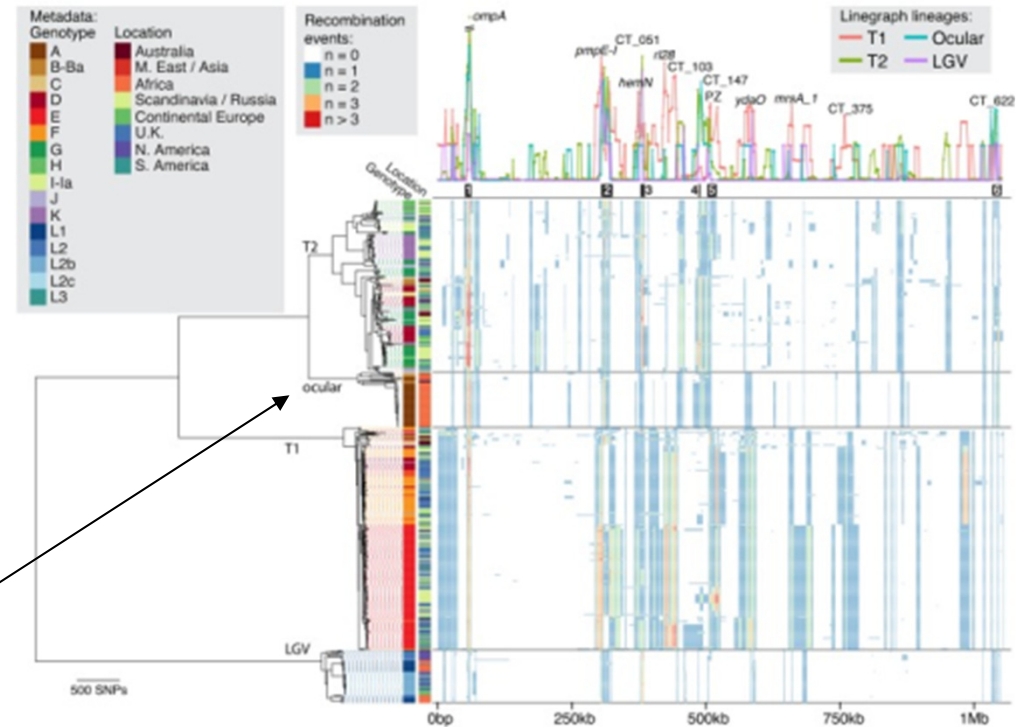
Ct genomics: current status

- Urogenital isolates constitute the majority of CT WGS
- 2017; 563 WGS published (Hadfield et al, 2017, *Genome Res*)

Research

Comprehensive global genome dynamics of *Chlamydia trachomatis* show ancient diversification followed by contemporary mixing and recent lineage expansion

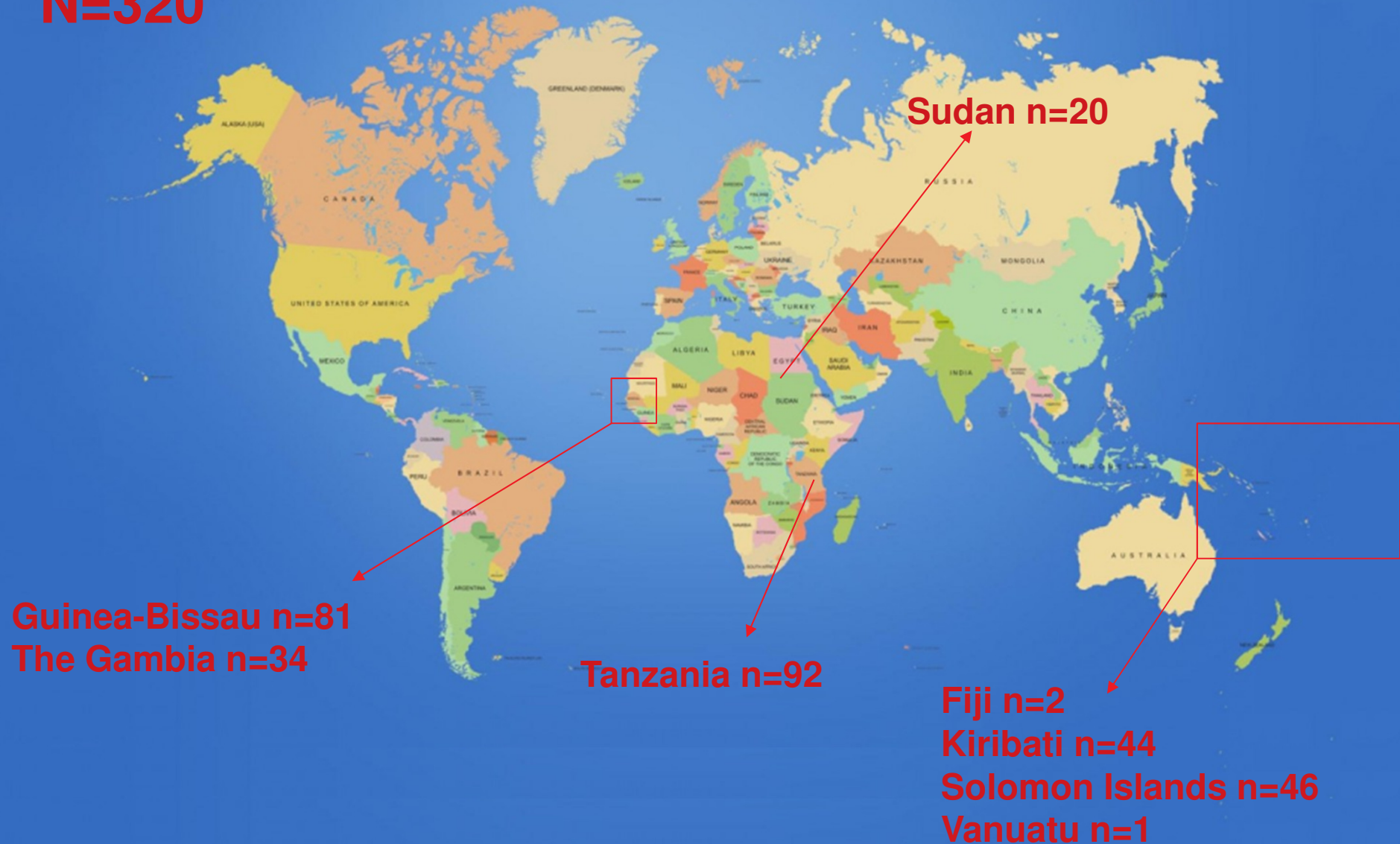
James Hadfield,¹ Simon R. Harris,¹ Helena M.B. Seth-Smith,^{1,24,25} Surendra Parmar,² Patiyon Andersson,³ Philip M. Giffard,^{3,4} Julius Schachter,⁵ Jeanne Moncada,⁵ Louise Ellison,¹ María Lucía Gallo Vaulet,⁶ Marcelo Rodríguez Fermepein,⁶ Frans Radebe,⁷ Suyapa Mendoza,⁸ Sander Ouburg,⁹ Servaas A. Morré,^{9,10} Konrad Sachse,¹¹ Mirja Puolakkainen,¹² Suvi J. Korhonen,¹² Chris Sonnex,² Rebecca Wiggins,¹³ Hamid Jalal,² Tamara Brunelli,¹⁴ Patrizia Casprini,¹⁴ Rachel Pitt,¹⁵ Cathy Ison,¹⁵ Alevtina Savicheva,¹⁶ Elena Shipitsyna,^{16,17} Ronza Hadad,¹⁷ Laszlo Kari,¹⁸ Matthew J. Burton,¹⁹ David Mabey,¹⁹ Anthony W. Solomon,¹⁹ David Lewis,^{7,20} Peter Marsh,²¹ Magnus Unemo,¹⁷ Ian N. Clarke,²² Julian Parkhill,¹ and Nicholas R. Thomson^{1,23}



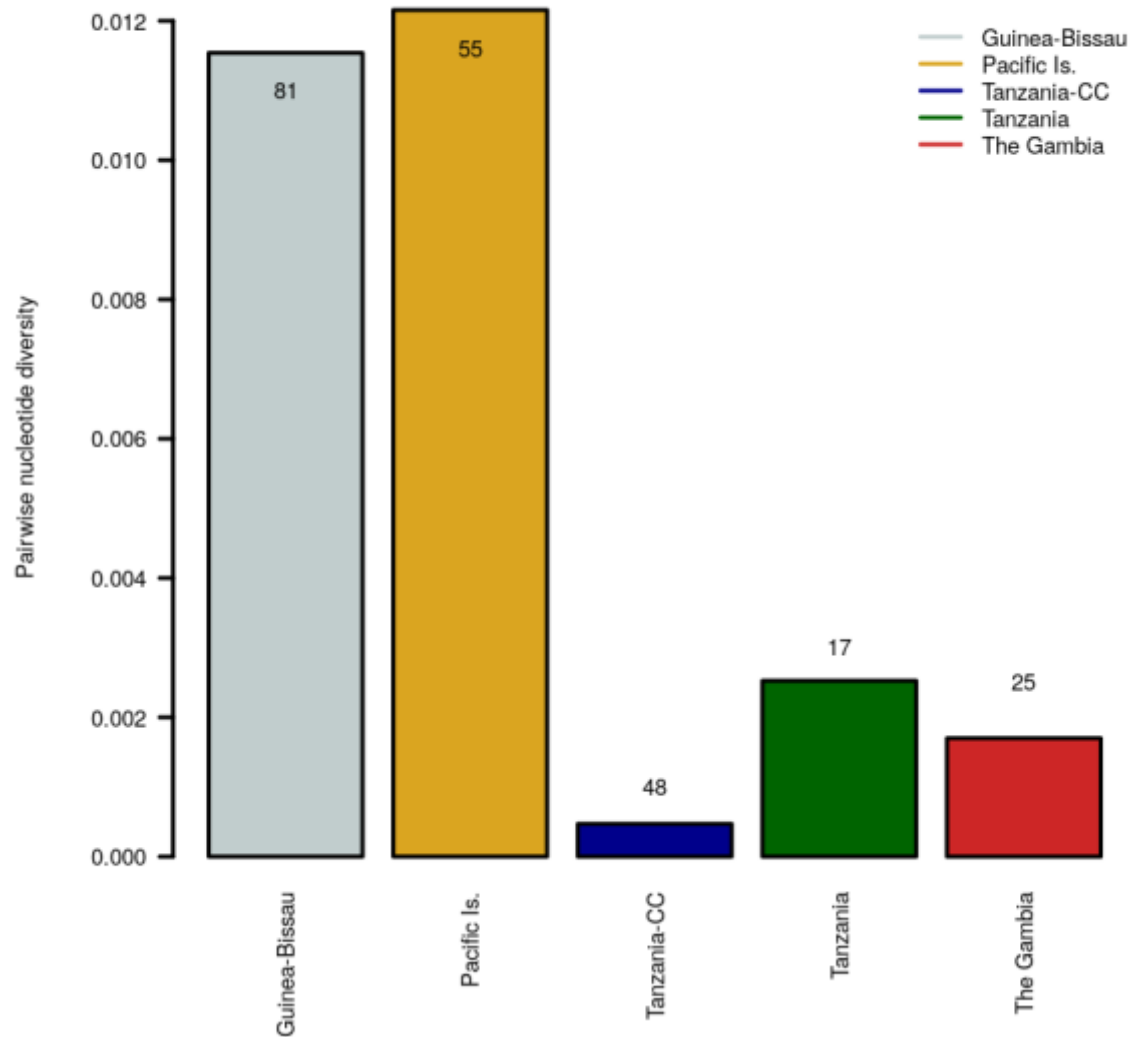
- 45 ocular isolates (< 8%)
 - 8 archived samples from 1950-2000
 - 37 clinical isolates from > 2000
- All underwent variable rounds of culture passage

Trachoma group WGS

N=320



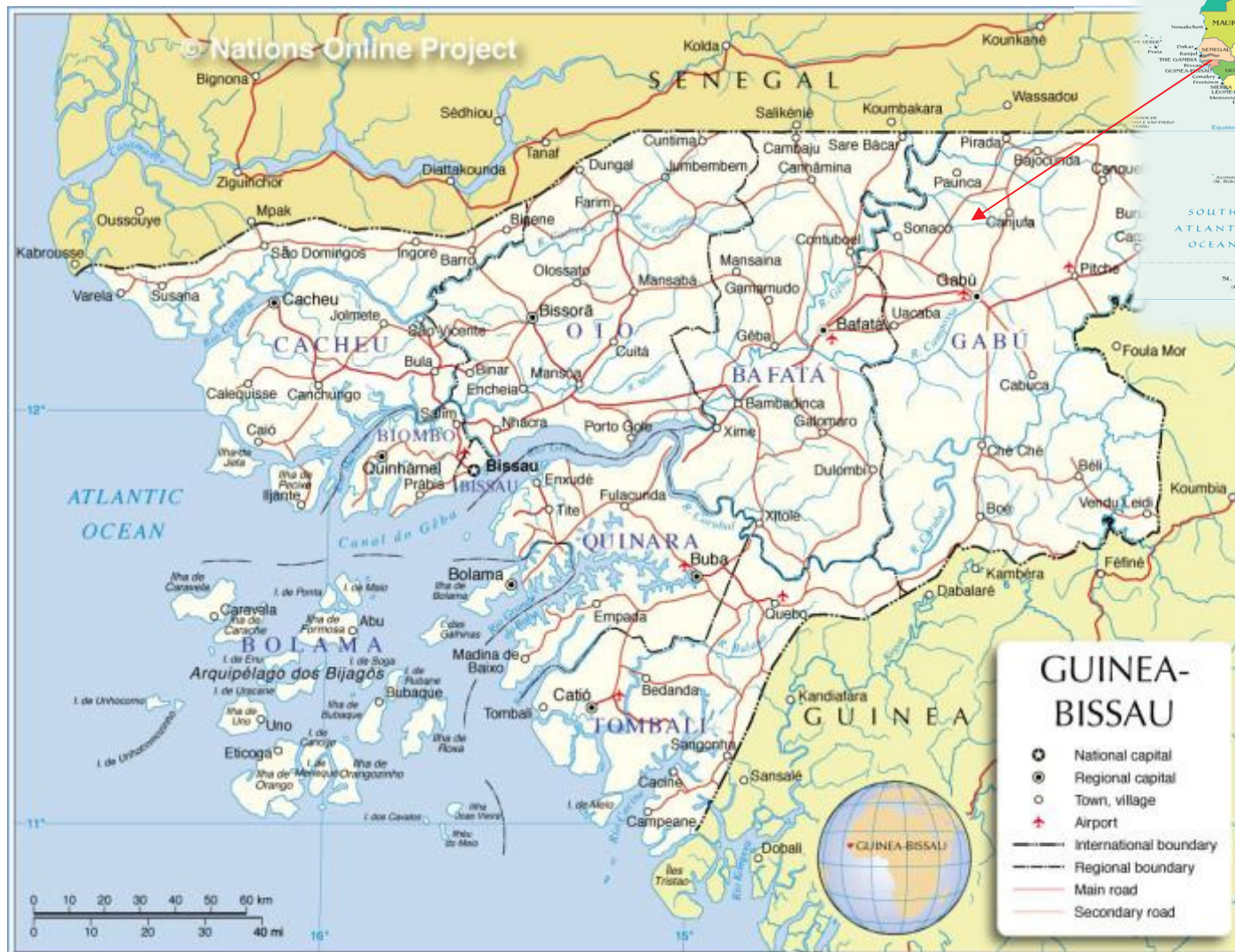
Population-level diversity



- Greater than expected diversity
- Considerable variation between populations
- Cell culture passage may reduce diversity

The Bijagos Archipelago

Last AR et al, 2014, *PloS Neglec Trop Dis*



1507 conjunctival swabs

220 Ct-positive samples

126 WGS

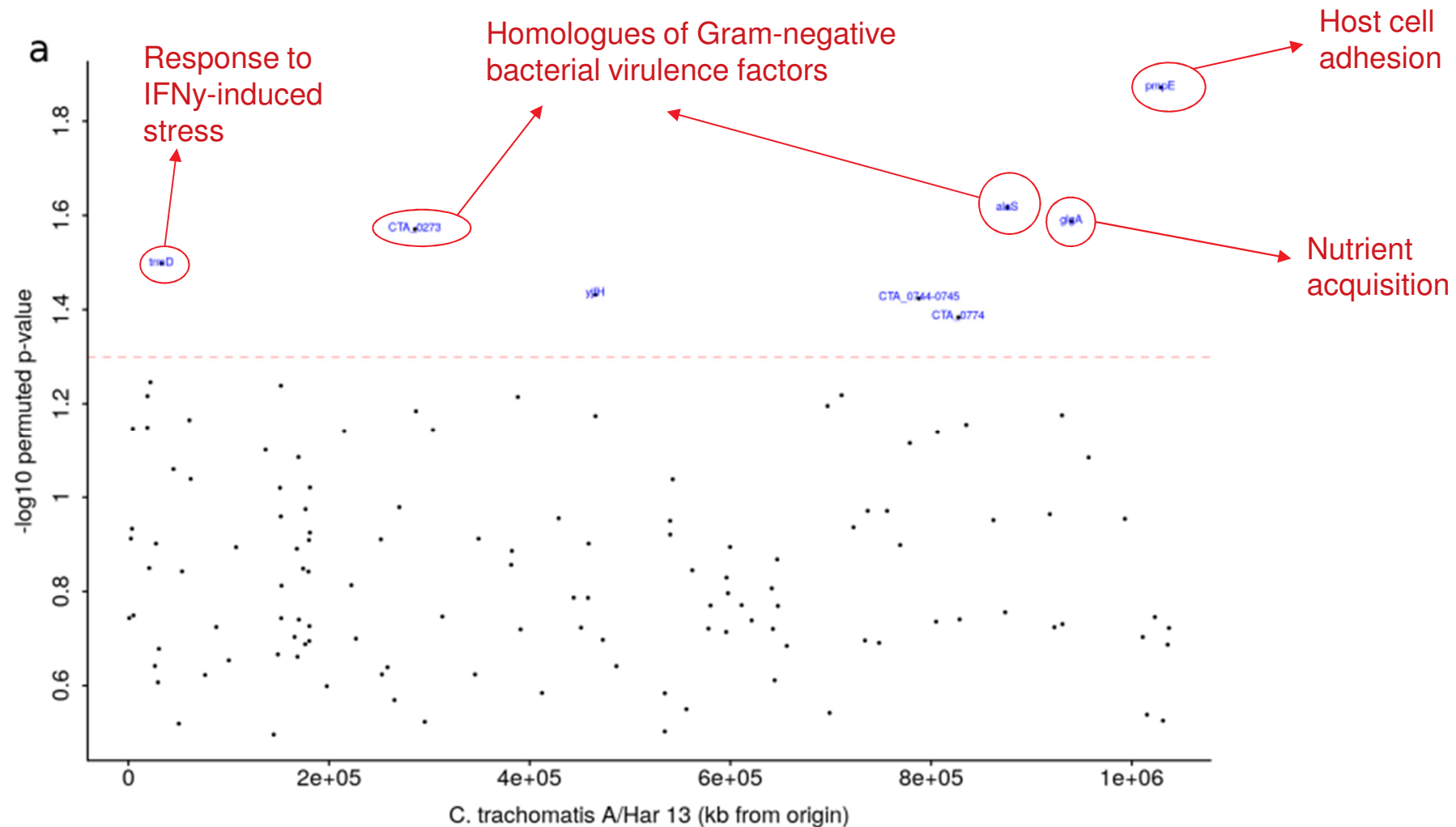
81 WGS in analyses

Genomics and pathogenicity



Last AR et al, 2018, *Gen Med*

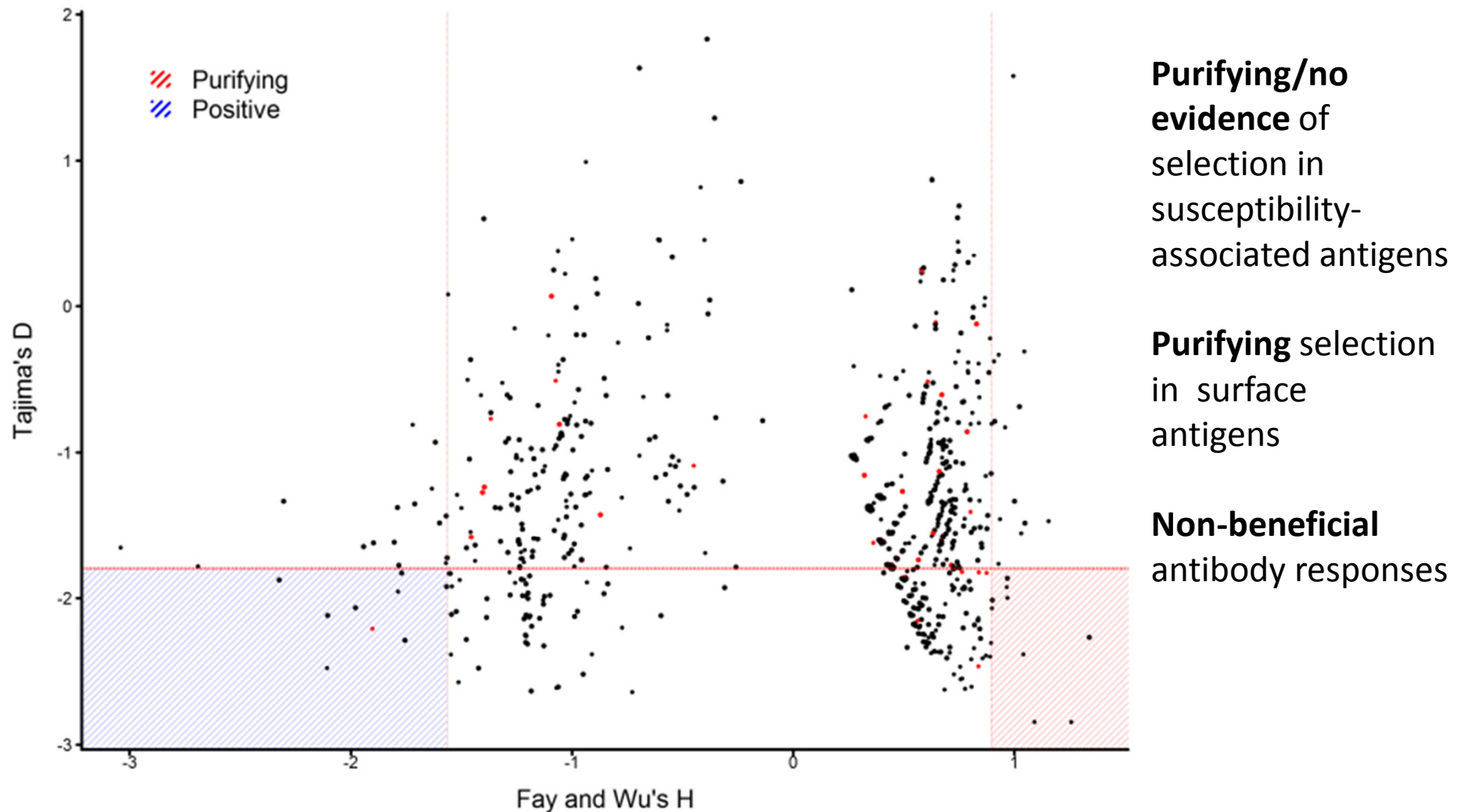
Identify SNPs associated with **disease severity** (inflammation and Ct load)



Genomics and immunity

Pickering H et al, 2017, *Sci Rep*

Identify patterns of selection in Ct antigens associated with susceptibility to infection



Uses for WGS in trachoma

Transmission and control

- Is population-level diversity related to endemicity?
- Does diversity impact success of MDA control efforts?
- Can WGS help understand patterns of transmission?

Pathogenicity

- Is diversity and/or genetic markers associated with Ct pathogenicity?
- Is diversity and/or genetic markers associated with disease severity?

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