

Towards a real-time genomic surveillance of arboviruses in the Americas



Nuno Rodrigues Faria

Sir Henry Dale, University of Oxford, UK

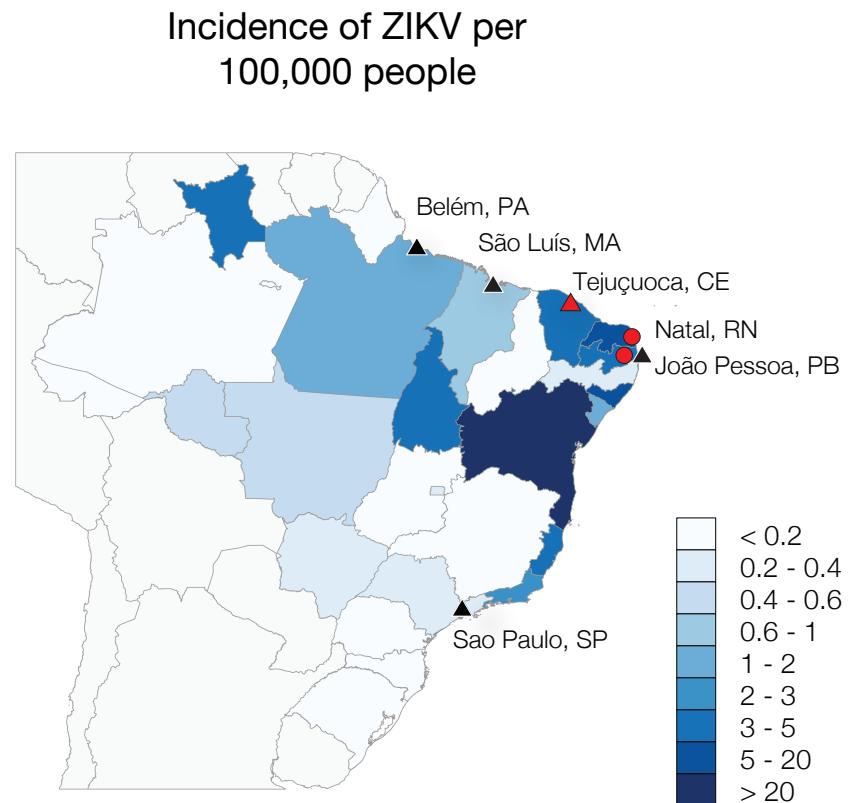
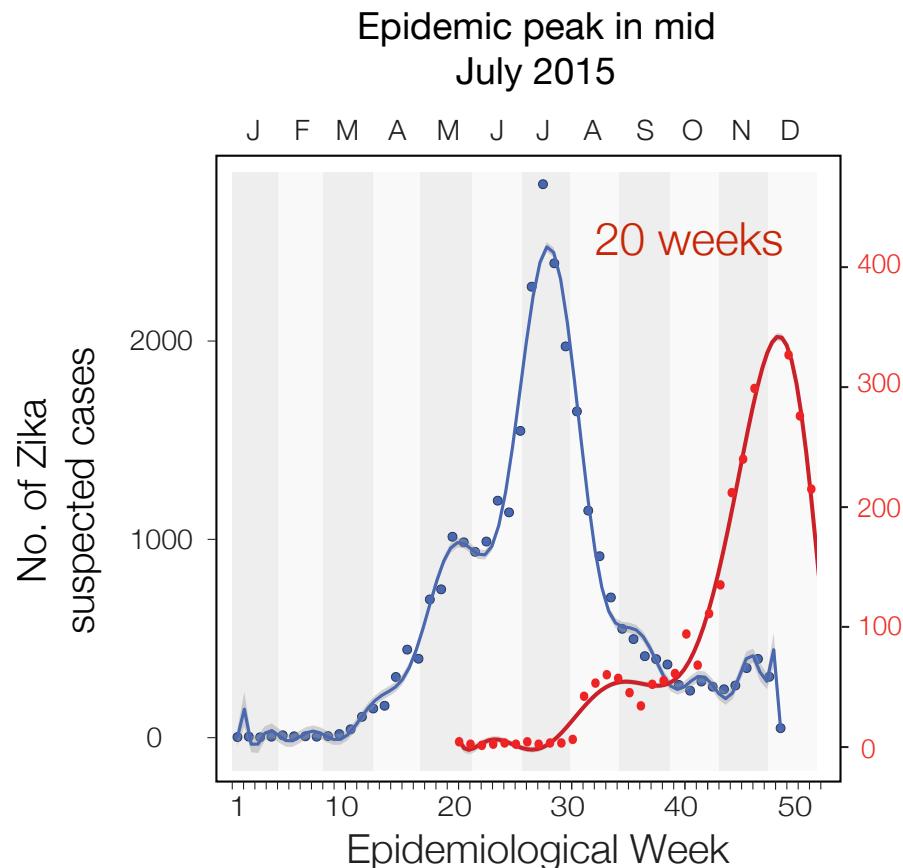
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Zika virus in Brazil and the Americas

Temporal association between ZIKV notified cases in 2015 and microcephaly

Local transmission in Brazil: 29 Apr 2015

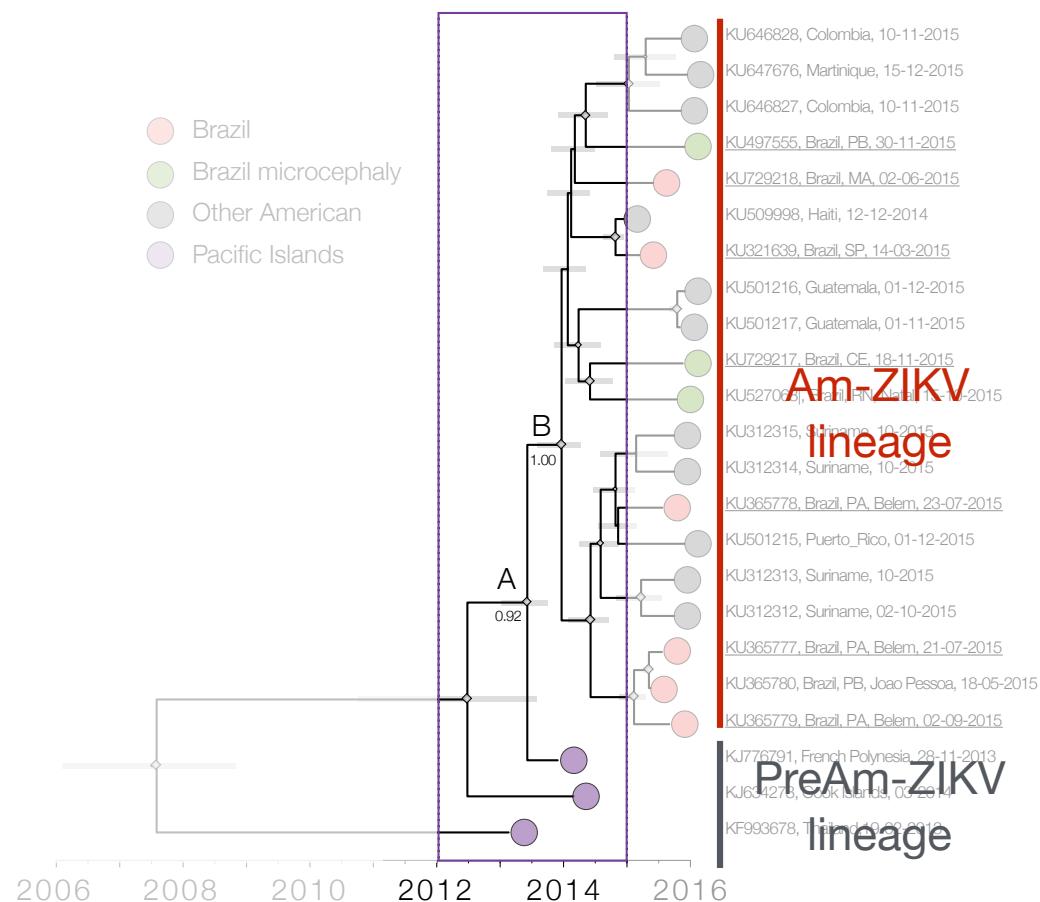
WHO Public Health Emergency of International Concern: 01 Feb 2016
WHO/CDC confirm association between ZIKV infection and **microcephaly**: 13 Apr 2016



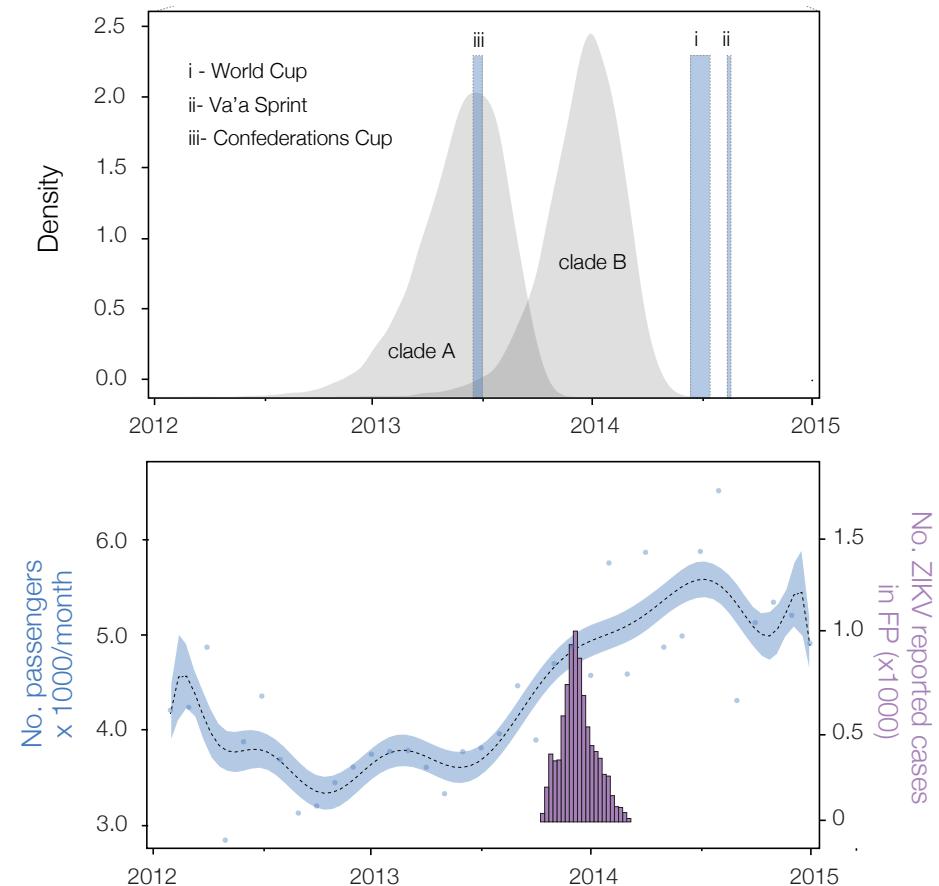
Faria et al. *Science* March 2016

Emergence of ZIKV as a function of local transmission regime, viral pathogenesis and global mobility

ZIKV Asian genotype
molecular clock phylogeny

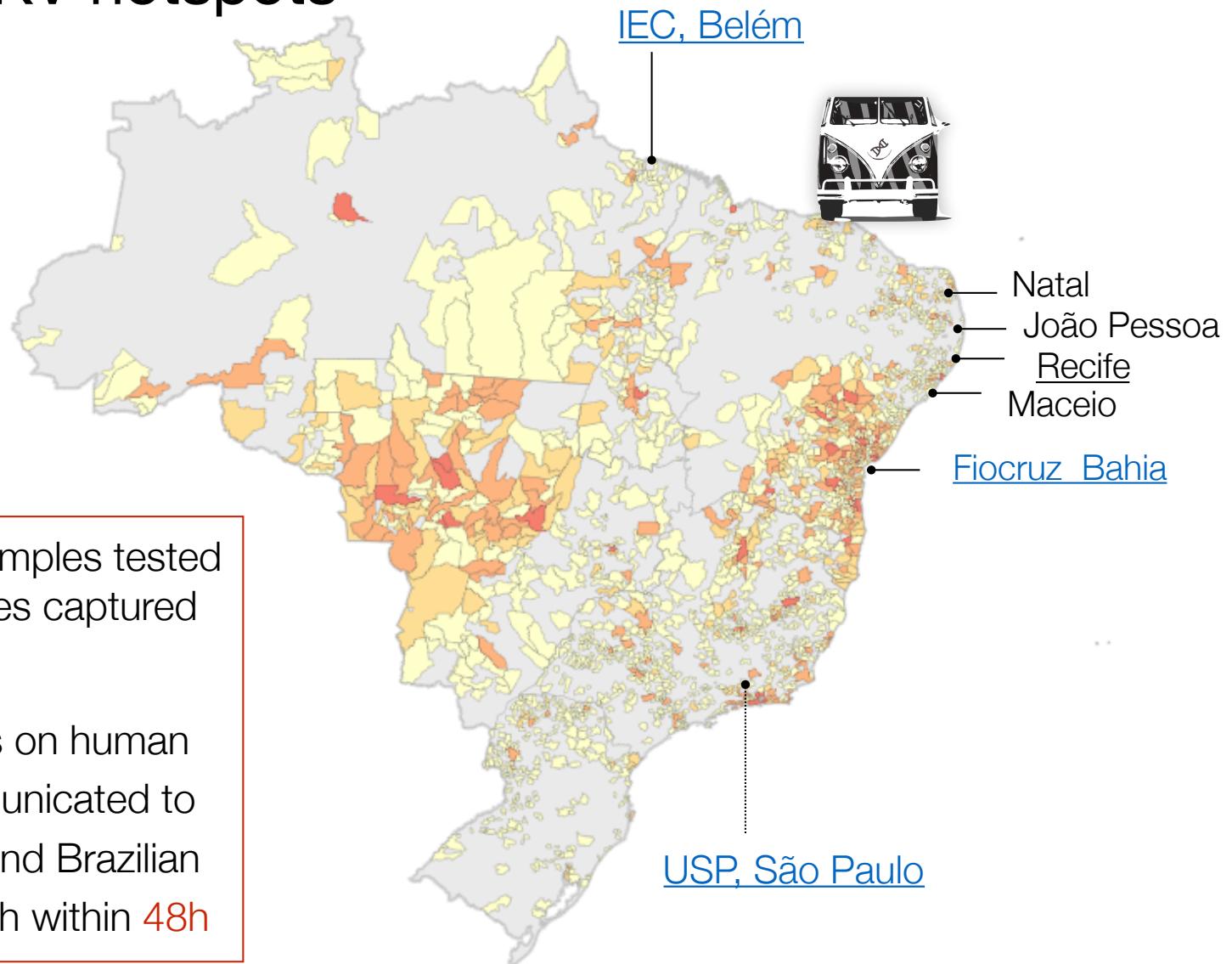


Combination of genetic
and flight data



The ZiBRA project, a sequencing journey through ZIKV hotspots

1330 human samples tested
838 mosquitoes captured
↓
RT-PCR results on human samples communicated to local LACENs and Brazilian Ministry of Health within **48h**



After the ZiBRA journey, molecular surveillance continued in SP and Bahia.

Zika virus real-time surveillance

Establishment and cryptic transmission of Zika virus in Brazil and the Americas

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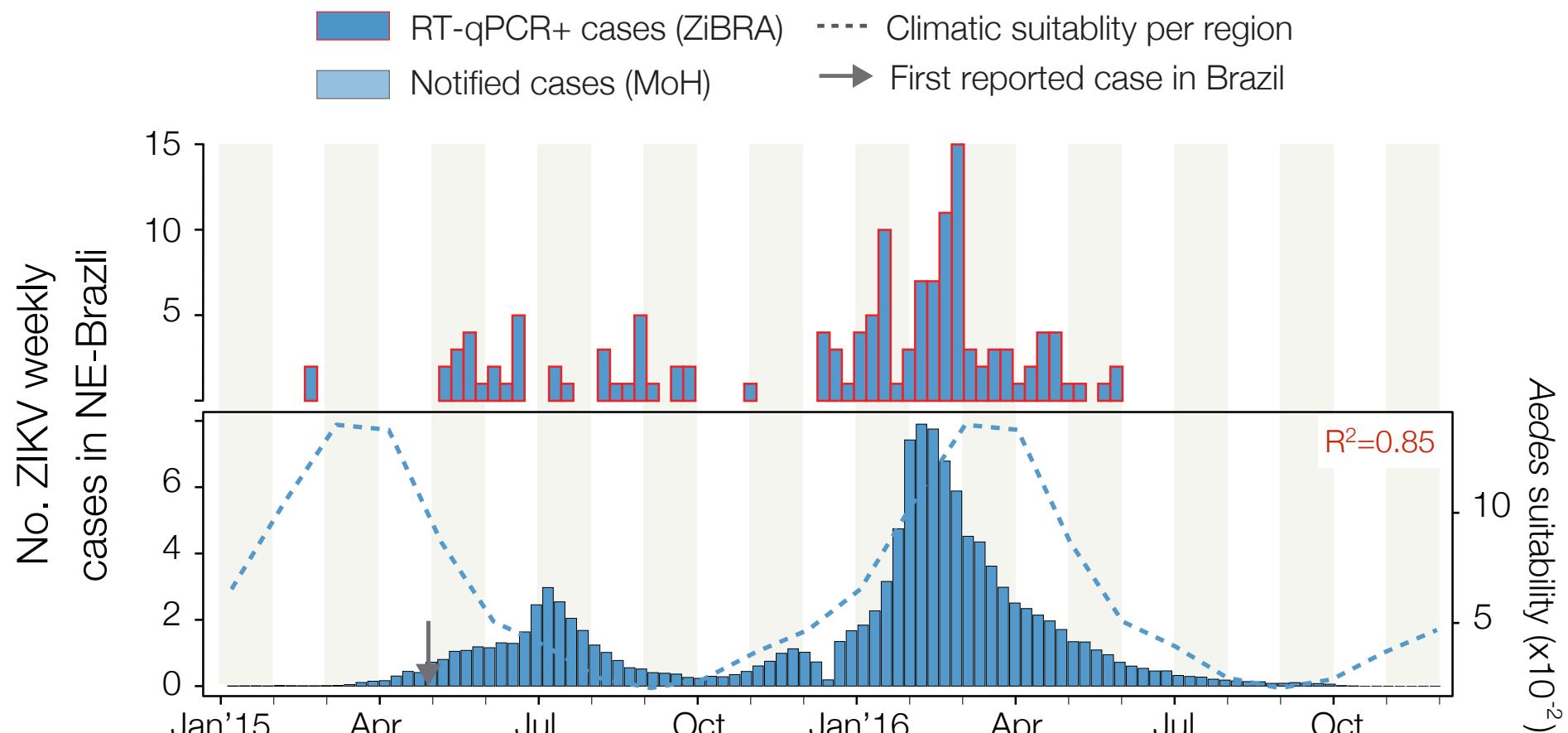
*These authors contributed equally to this work.

§These authors jointly supervised this work.



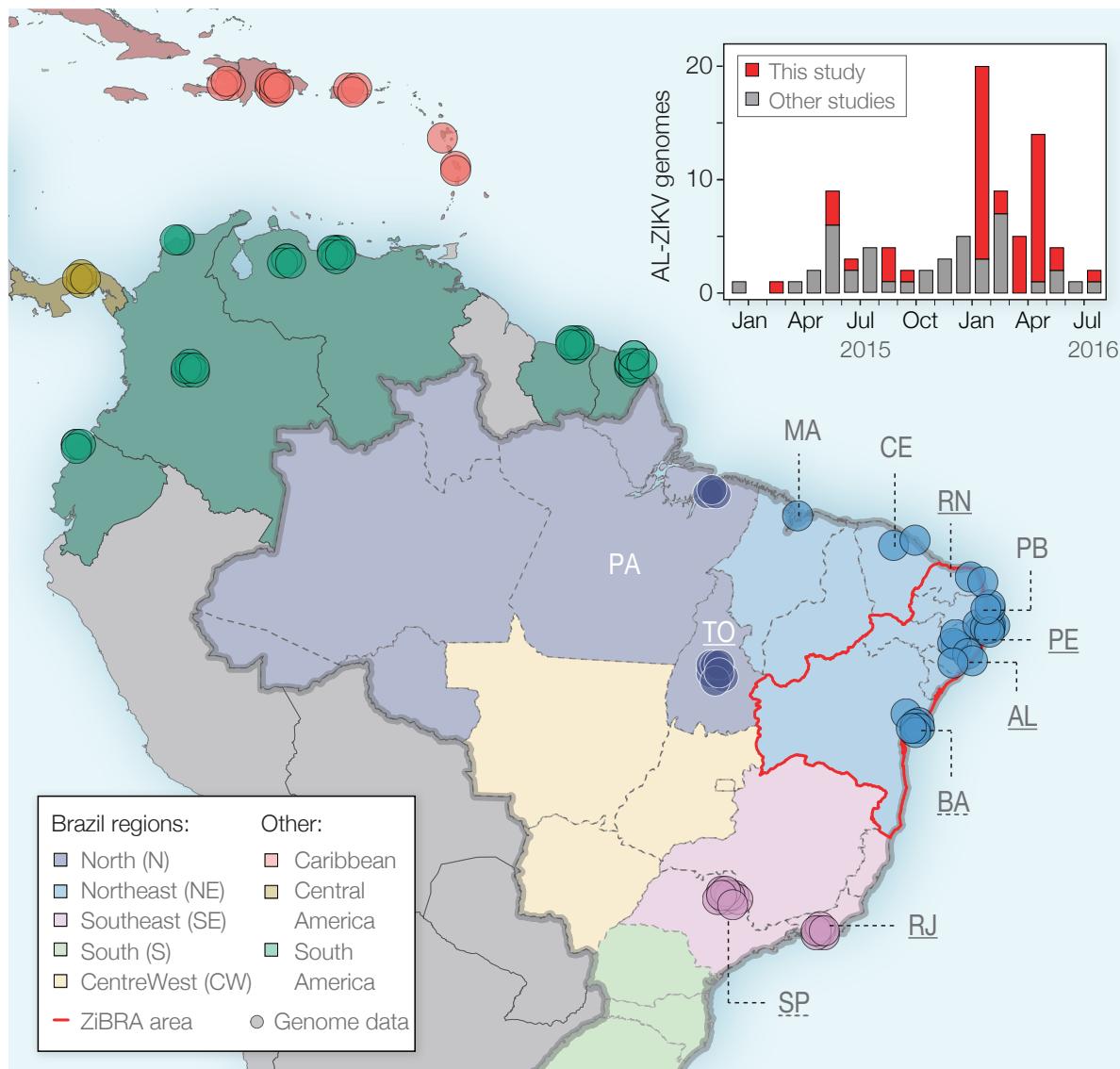


Zika virus MoH notified cases is positively associated with Zika RT-qPCR+ cases **and climatic suitability**



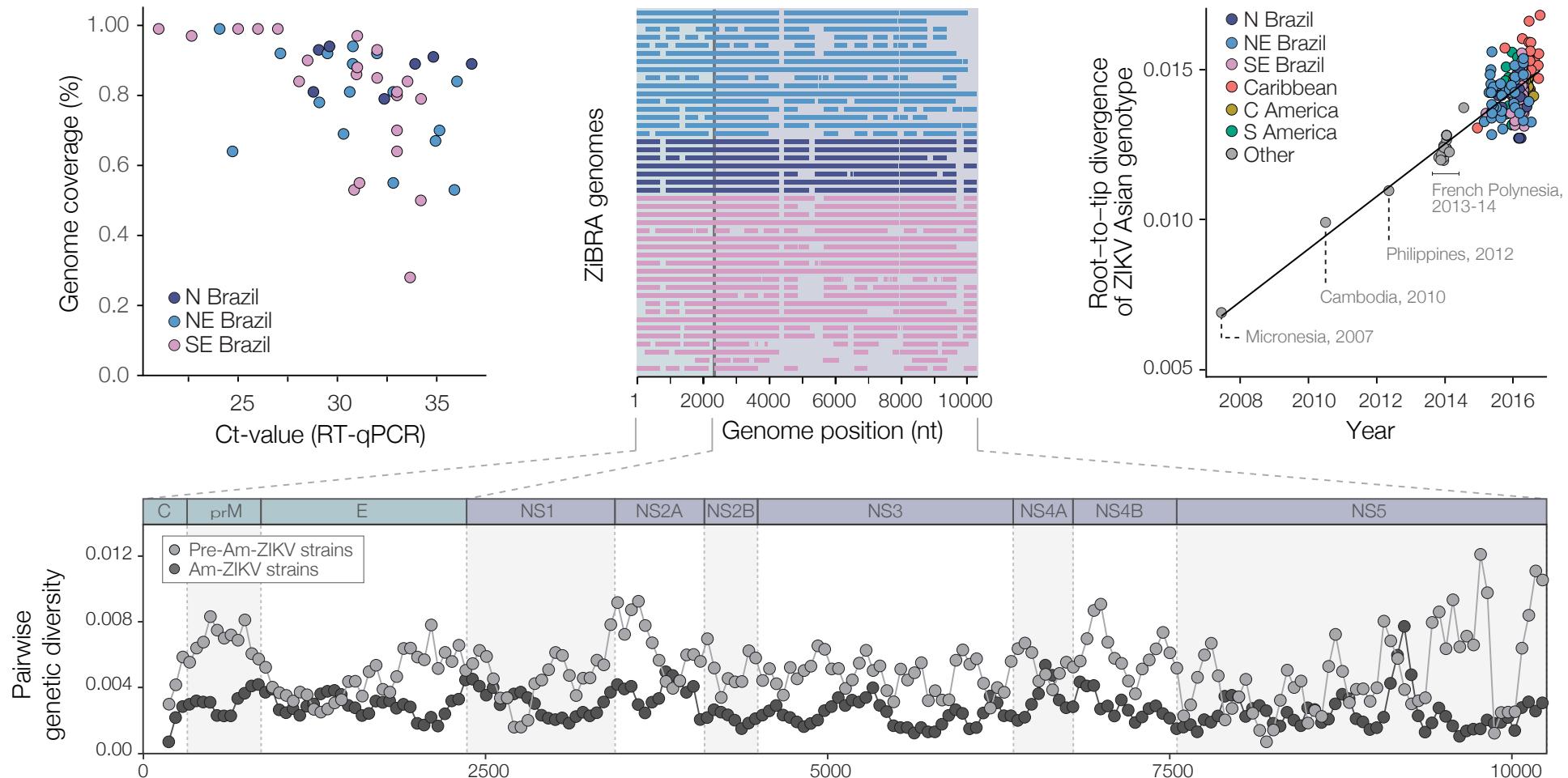
Can we predict when an epidemic will occur based on climatic factors?

Genome-wide analysis of ZiBRA genetic data*



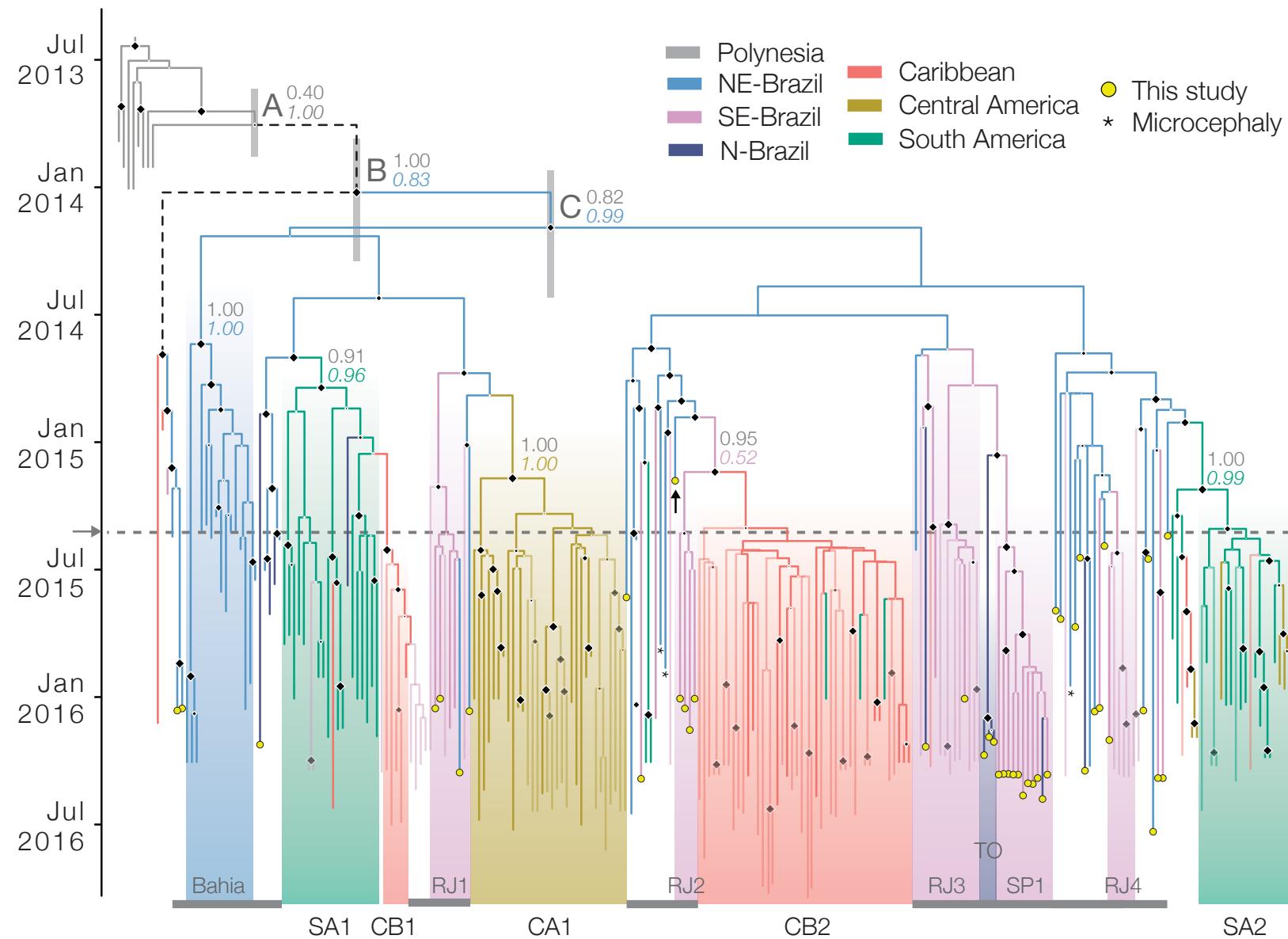
*Nearly half (47%) of all published genomes until Feb 2017

Genomic diversity of PreAm-ZIKV and Am-ZIKV lineages

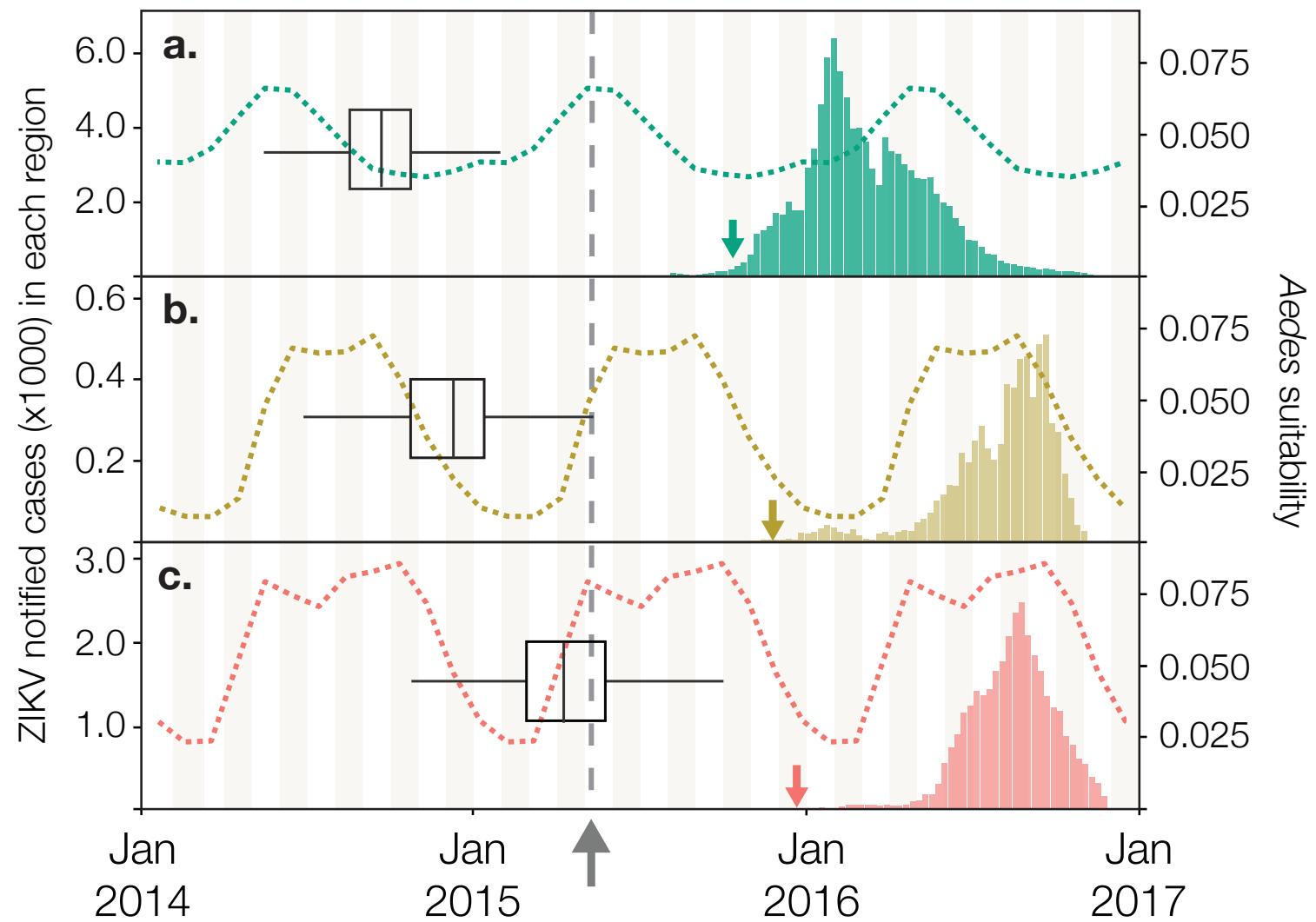


Faria et al. *Nature* May 2017

Origins of ZIKV-AL in northeast Brazil, from where it spread to southeast Brazil and beyond



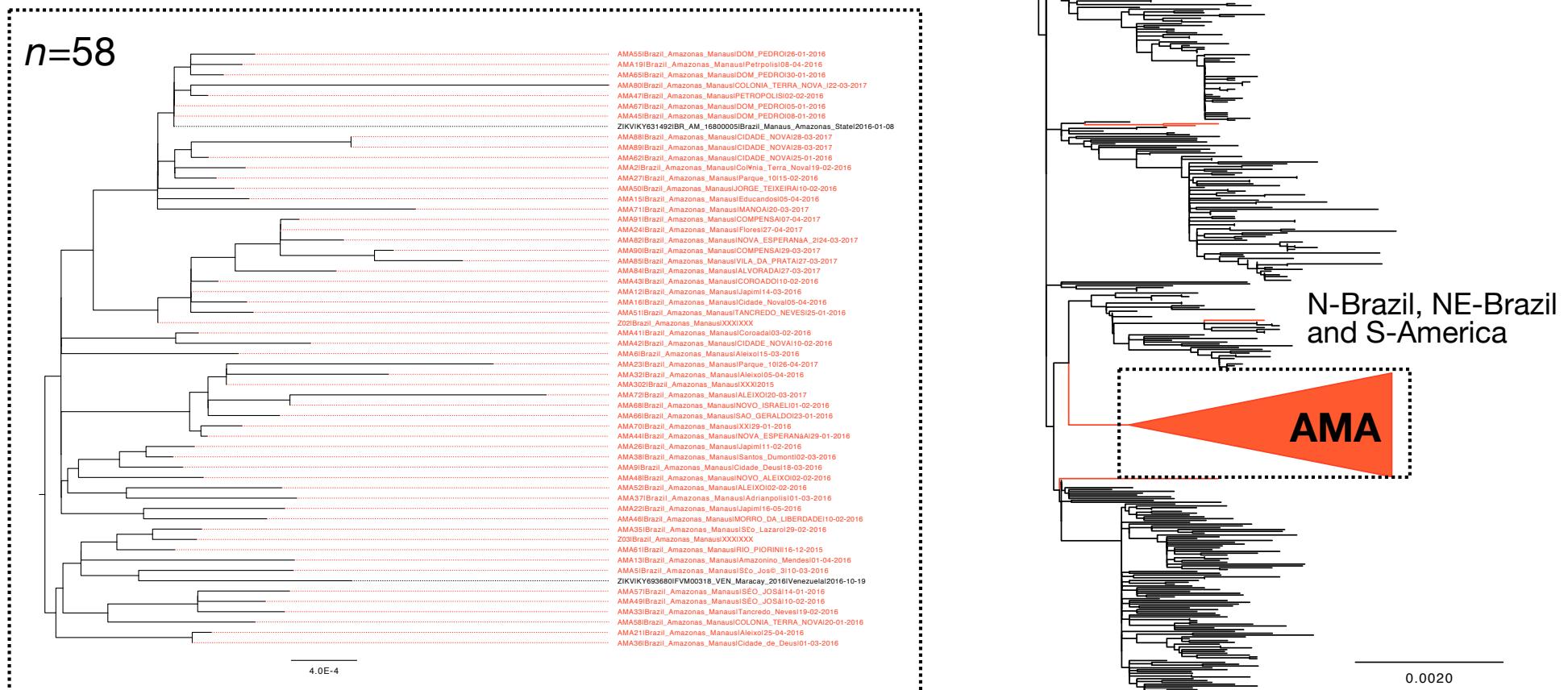
Cryptic circulation in several American regions for a near-complete season of transmission



Faria et al. *Nature* May 2017

ZiBRA2 data: one predominant introduction of Zika virus in Manaus, capital city of Amazonas

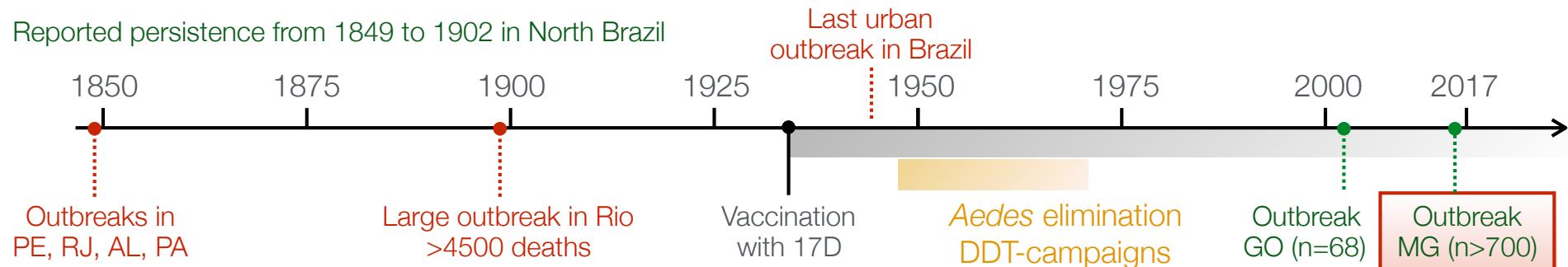
Total of 62 new ZIKV genomes generated in 7d



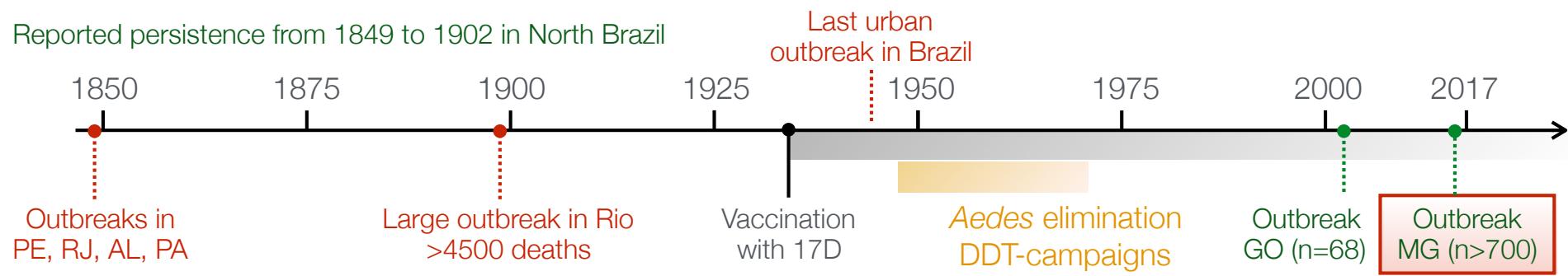
In prep. 2017

Yellow fever virus real-time surveillance during the outbreak in Minas Gerais

Natural history of the yellow fever virus in Brazil

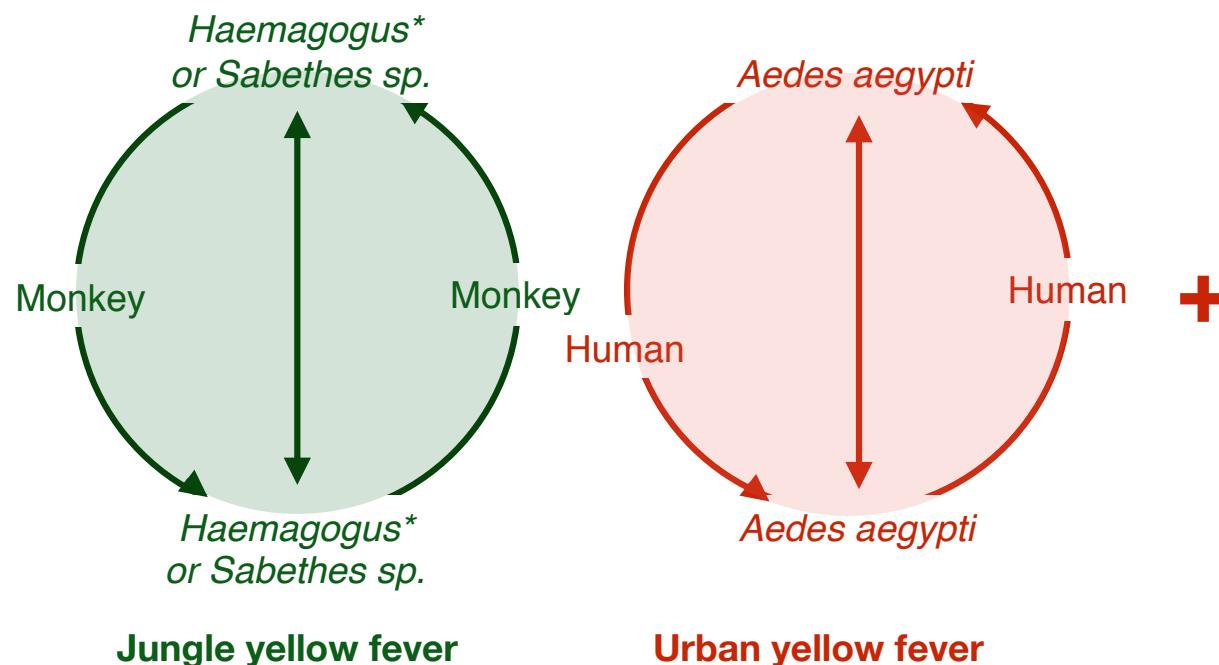


Natural history of the yellow fever virus in Brazil

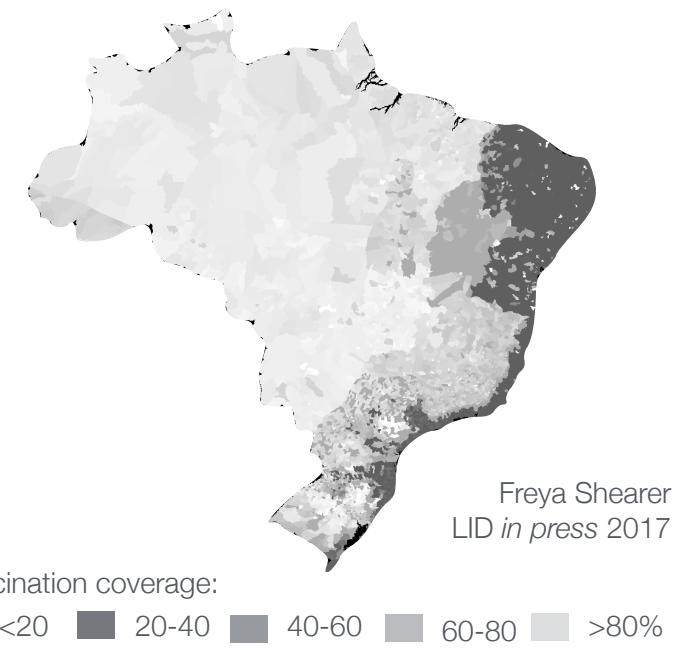


Vainio & Cutts,
WHO 1981

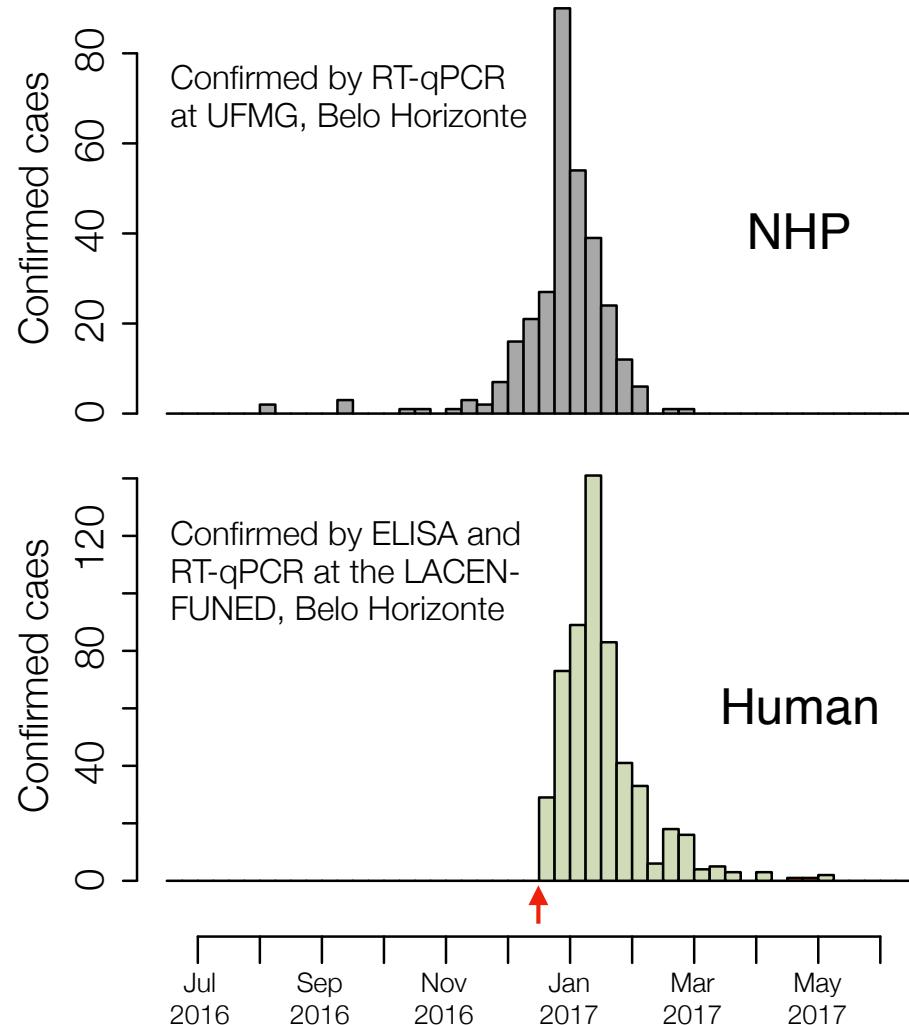
Transmission cycles in South America



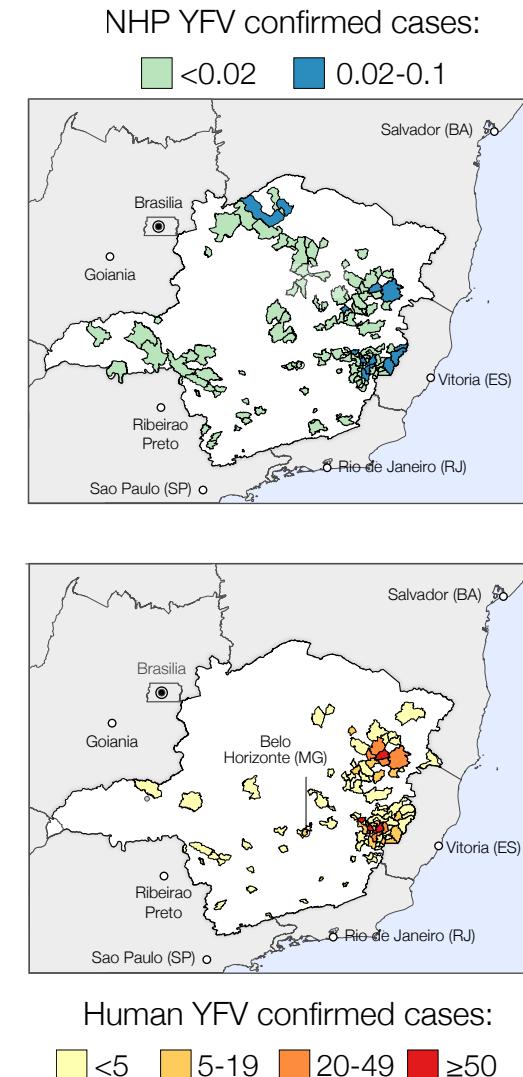
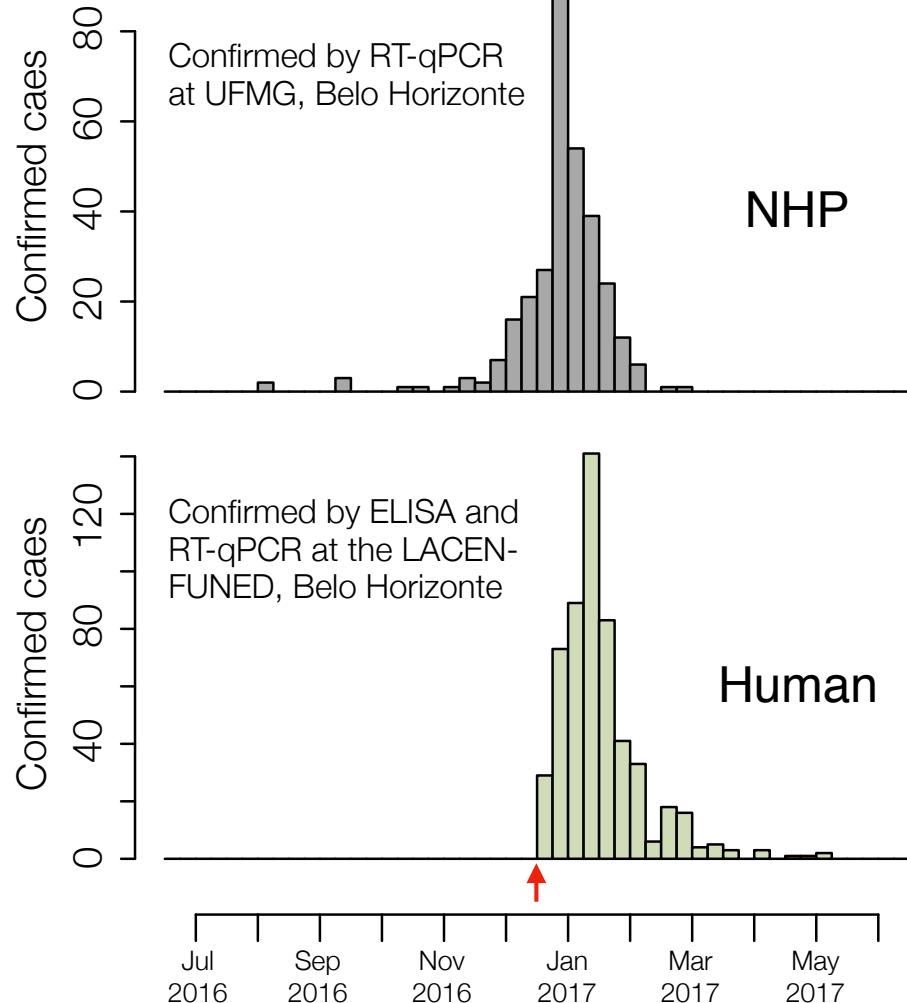
Yellow Fever vaccination coverage Brazil 2016



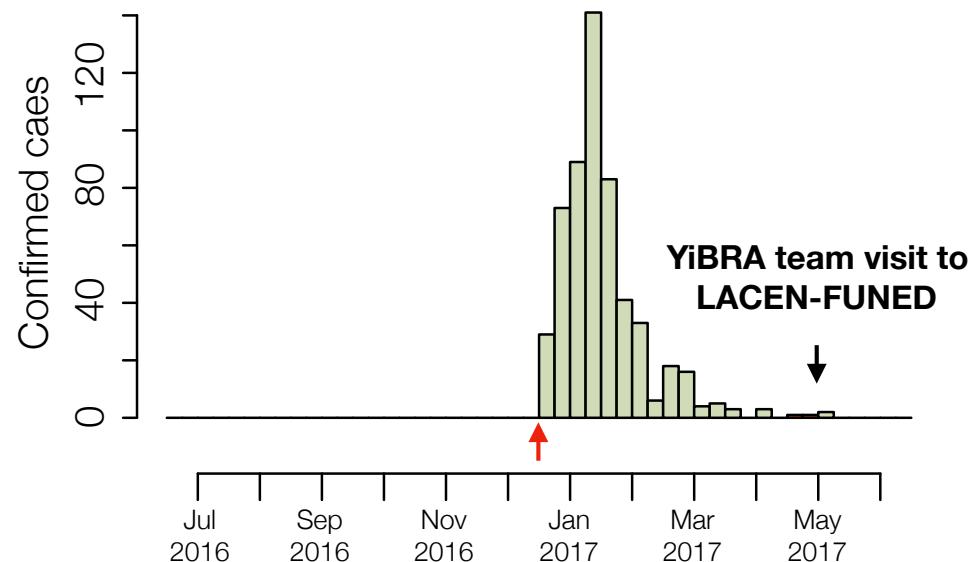
Temporal association between cases in non-human primates and humans



Temporal and spatial association between cases in non-human primates and humans

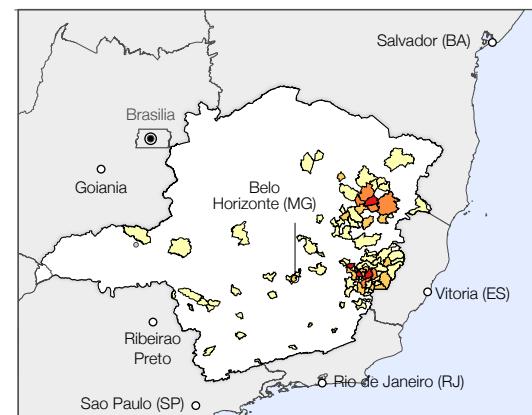
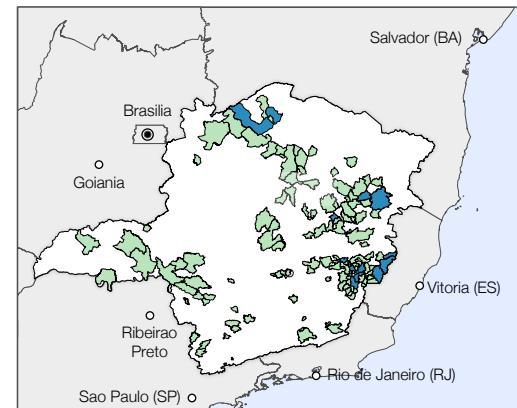


Temporal and spatial association between cases in non-human primates and humans



NHP YFV confirmed cases:

<0.02 0.02-0.1



Human YFV confirmed cases:

<5 5-19 20-49 ≥50



Genomic diversity of circulating YFV lineages?

Vaccine design & diagnostic methods

Evolutionary origins of the ongoing outbreak in Minas Gerais (MG)?

-> insight into timing, source location and transmission cycle

Patterns and drivers of virus spread in different MG host populations?

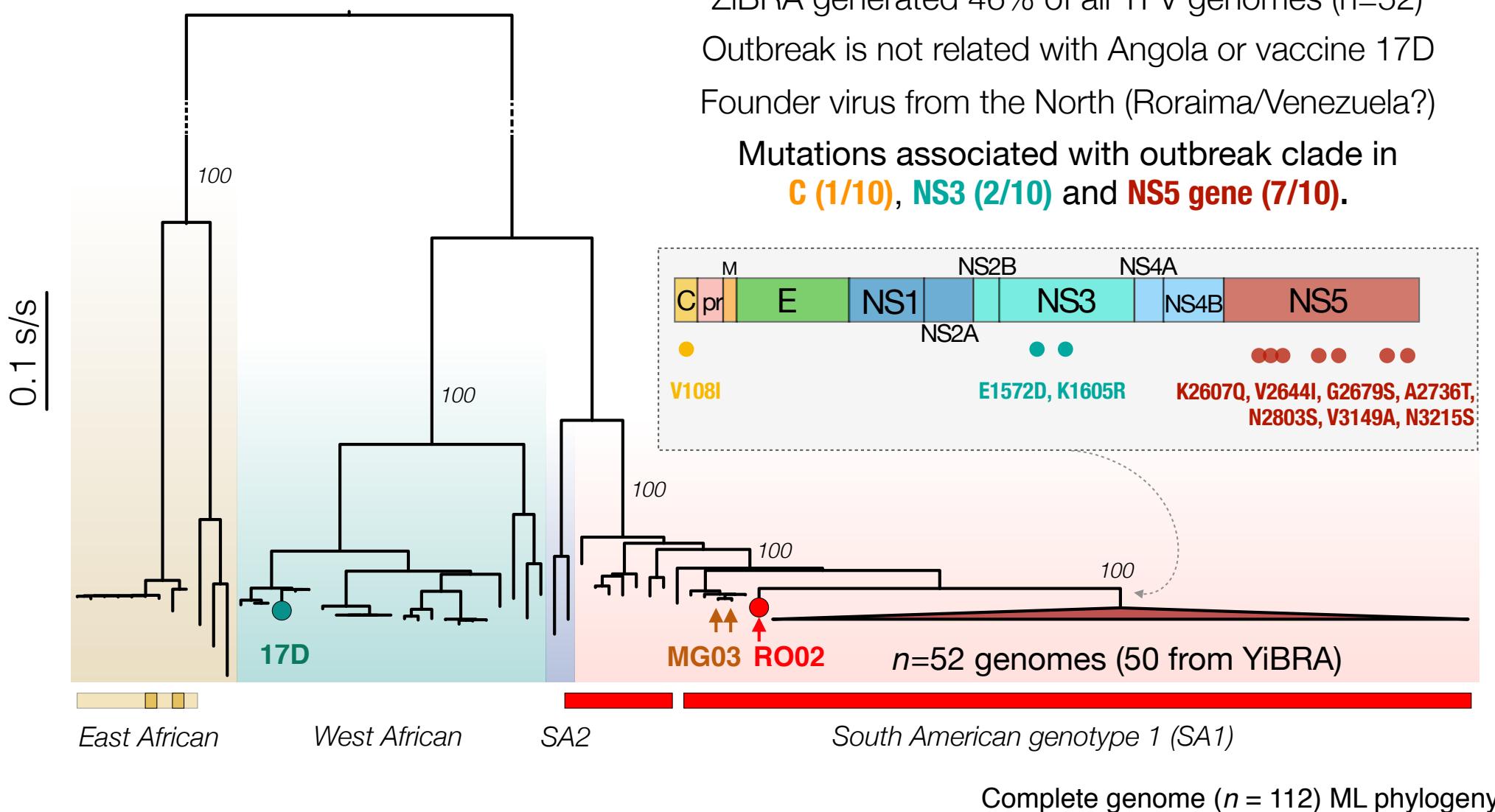
-> Build predictive models virus spread and forecasting

Are there associations between changes in YFV genome
and disease severity such as death?

No such associations have been found yet, but
currently there are only 2 genomes available

Is there any ecological and/or evolutionary explanation for
the magnitude of the recent outbreak?

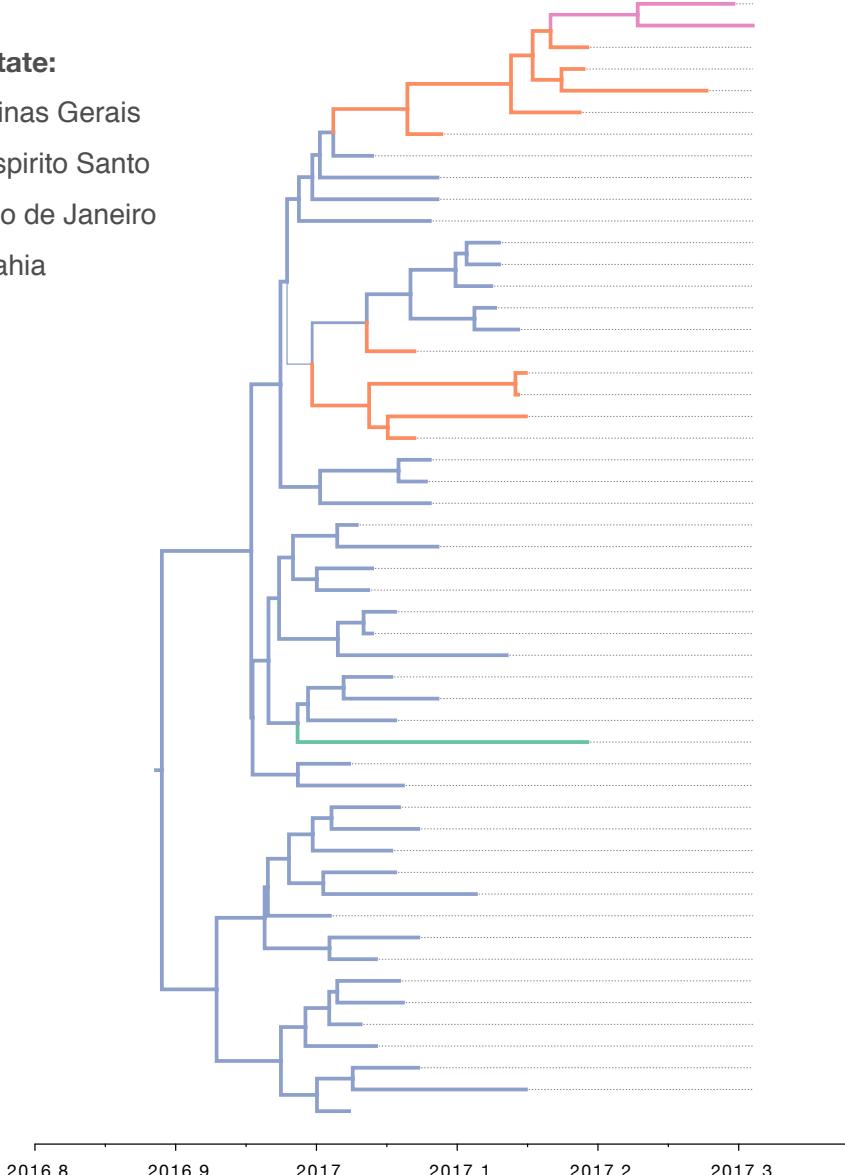
Genomic epidemiology of the YFV outbreak in Minas Gerais, Brazil



Genomic epidemiology of the YFV outbreak in Minas Gerais, Brazil

Federal state:

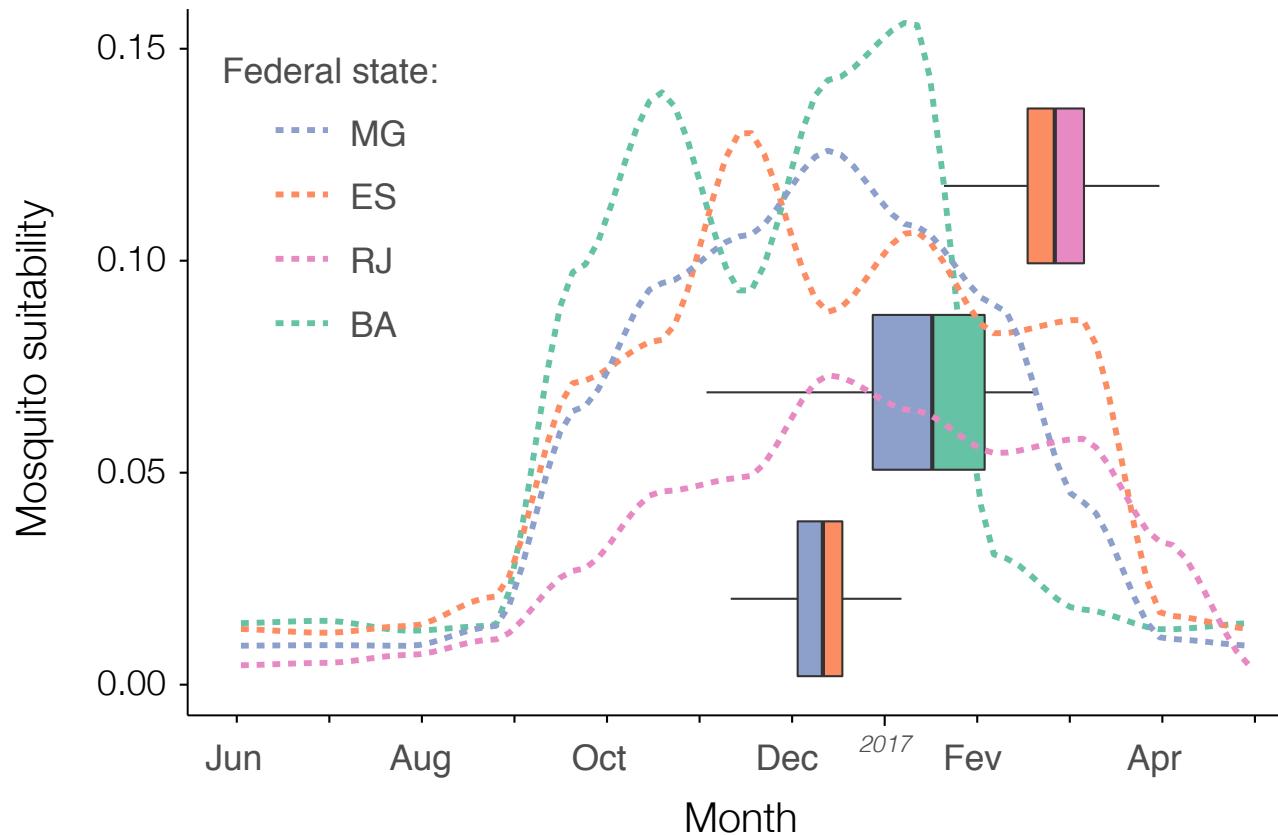
- Minas Gerais
- Espírito Santo
- Rio de Janeiro
- Bahia



FioRJ	FioRJ14278 Monkey RioJaneiro_Marical17-04-2017
FioRJ	FioRJ14480 Human RioJaneiro_CasimirodeAbreu12-04-2017
FioRJ	FioRJ18181 Human EspiritoSanto_Cariacical10-03-2017
FioRJ	FioRJ12115 Monkey EspiritoSanto_Cariacical09-03-2017
FioRJ	FioRJ13919 Human EspiritoSanto_DomingosMartins10-04-2017
FioRJ	FioRJ12109 Monkey EspiritoSanto_Cariacical08-03-2017
FioRJ	FioRJ14381 Monkey Espirito_Santo_DomingosMartins31-01-2017
FioRJ	FioRJ15321 Monkey MinasGerais_CoronelMurtal13-01-2017
FioRJ	FioRJ14651 Human MinasGerais_Itambacuril30-01-2017
FioRJ	FioRJ14601 Human MinasGerais_NovoCruzeiro130-01-2017
FioRJ	FioRJ14801 Human MinasGerais_TeofiloOtonil28-01-2017
FUNED	M91 Primate MinasGerais_OuroFino15-02-2017
FUNED	M51 Primate MinasGerais_SantaRitaDeCaldas15-02-2017
FUNED	M11 Primate MinasGerais_Caldas13-02-2017
FUNED	M71 Primate MinasGerais_Delfinopolis14-02-2017
FUNED	M78 Primate MinasGerais_Claravall20-02-2017
IAL	IAL_11 Primate EspiritoSanto_VendaNovadaImigrante12-01-2017
-	NCIES505 NHP Primate DomingosMartins EspiritoSanto22-02-2017
-	NCIES504 NHP Primate DomingosMartins EspiritoSanto20-02-2017
FioRJ	FioRJ15361 Human EspiritoSanto_Vitorial22-02-2017
IAL	IAL_8 Primate EspiritoSanto_Itarana12-01-2017
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FUNED	M164 Human MinasGerais_Simoesia130-01-2017
FUNED	M94 Human MinasGerais_ImbeDeMinas13-01-2017
FUNED	M105 Human MinasGerais_PiedadeCaratingal12-01-2017
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FUNED	M47 Human MinasGerais_Setubinal19-01-2017
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FUNED	M18 Human MinasGerais_Itambacuril21-01-2017
FUNED	M138 Human MinasGerais_SantaBarbaradoLestel20-01-2017
FUNED	M216 Primate MinasGerais_ZonaDaMatal25-01-2017
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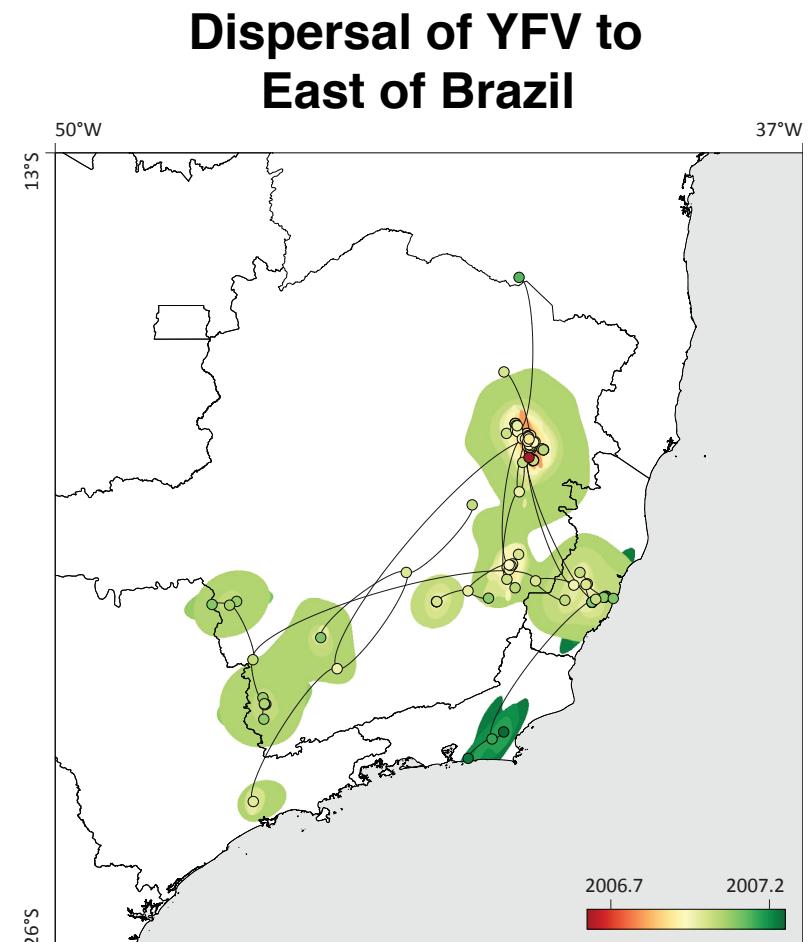
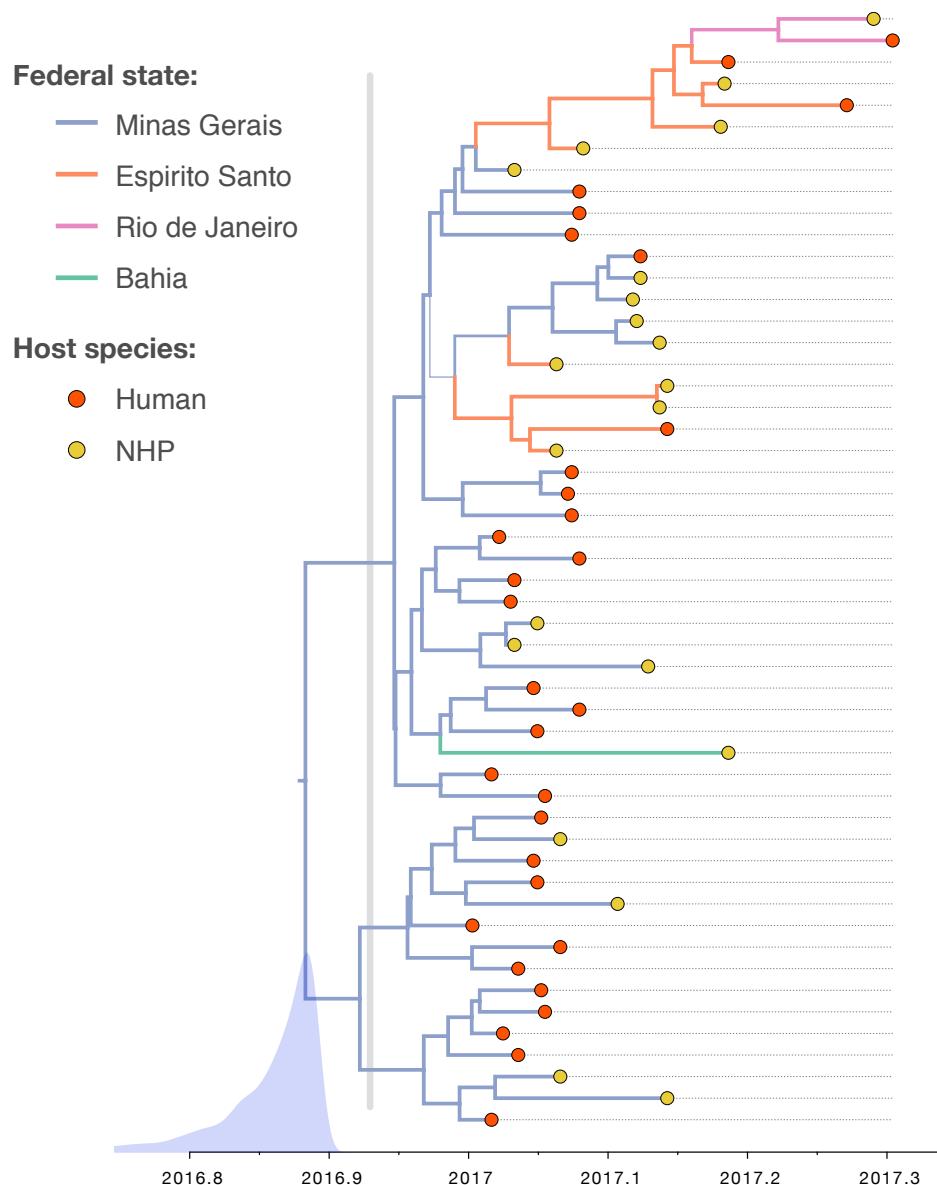
Yellow fever outbreak

Dating earliest introductions in neighbour states to Minas Gerais



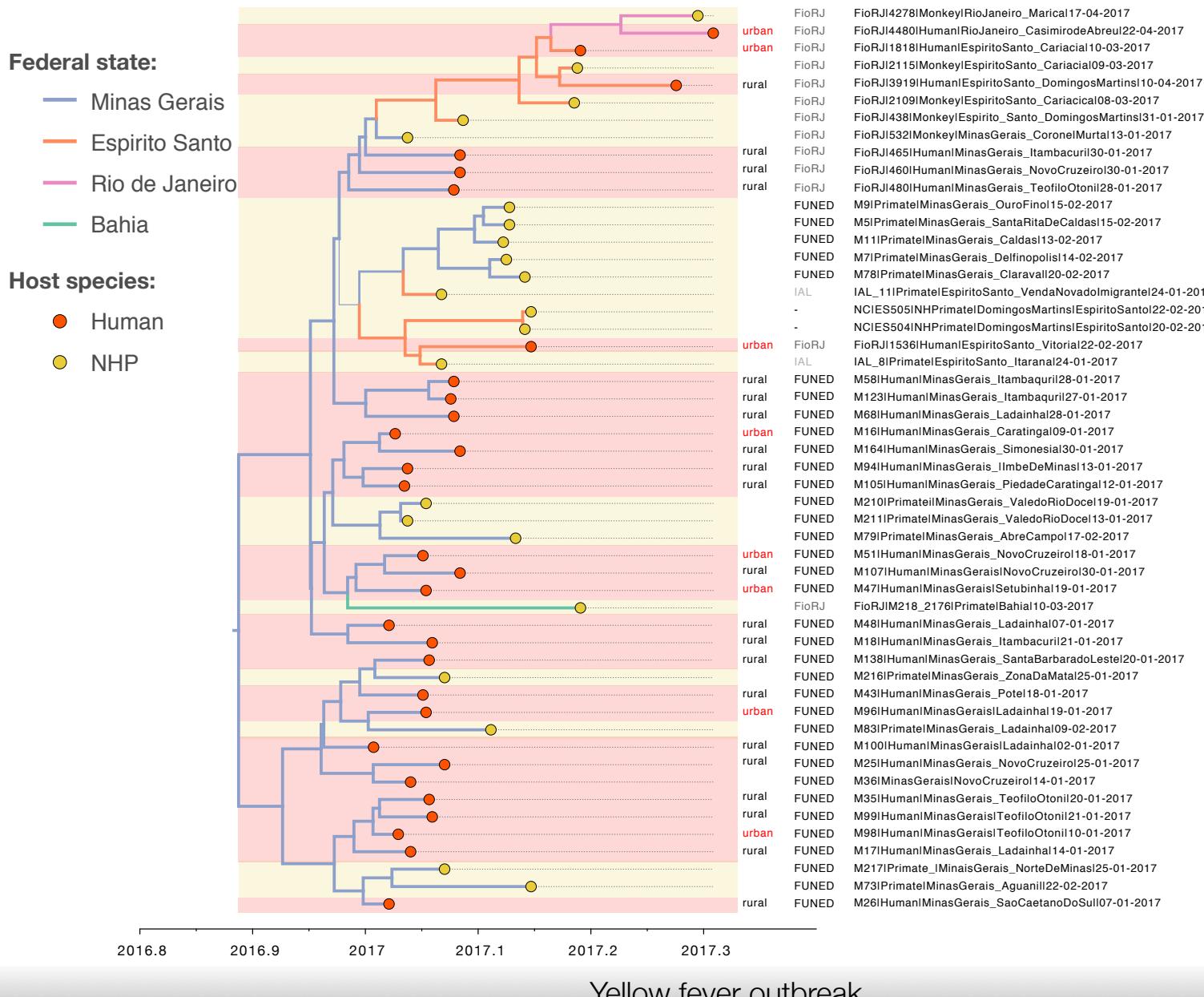
Exportation of YFV lineages from MG to other states happened in period of low climatic suitability in recipient states, specially in Rio de Janeiro and Bahia

Dispersal of YFV to the southeast region of Brazil



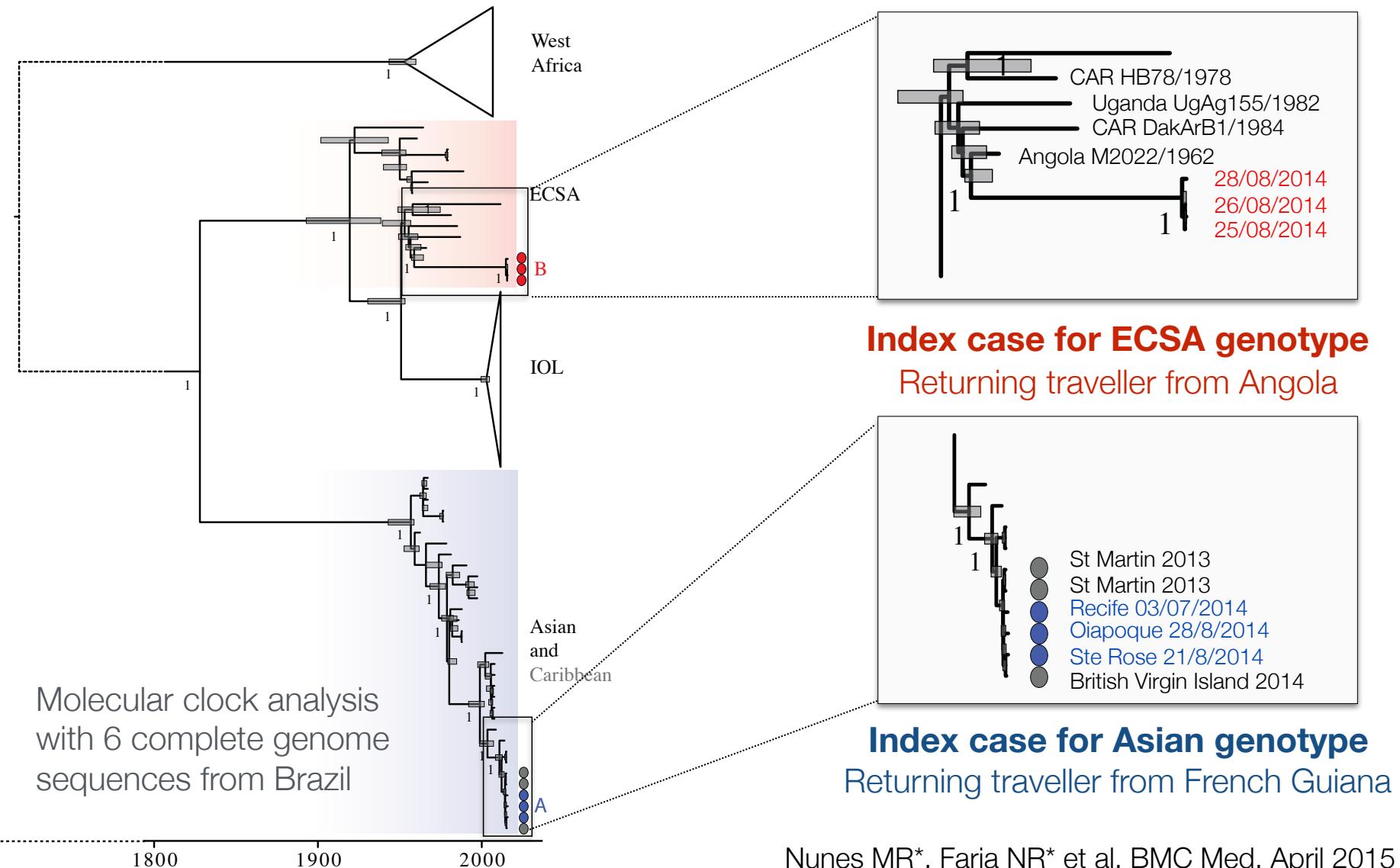
Continuous diffusion model
Seraphim (by Dellicour S.)

Current genetic data does not support YFV urban transmission (yet?)



Origins and spread of the Chikungunya ECSA genotype in the Americas

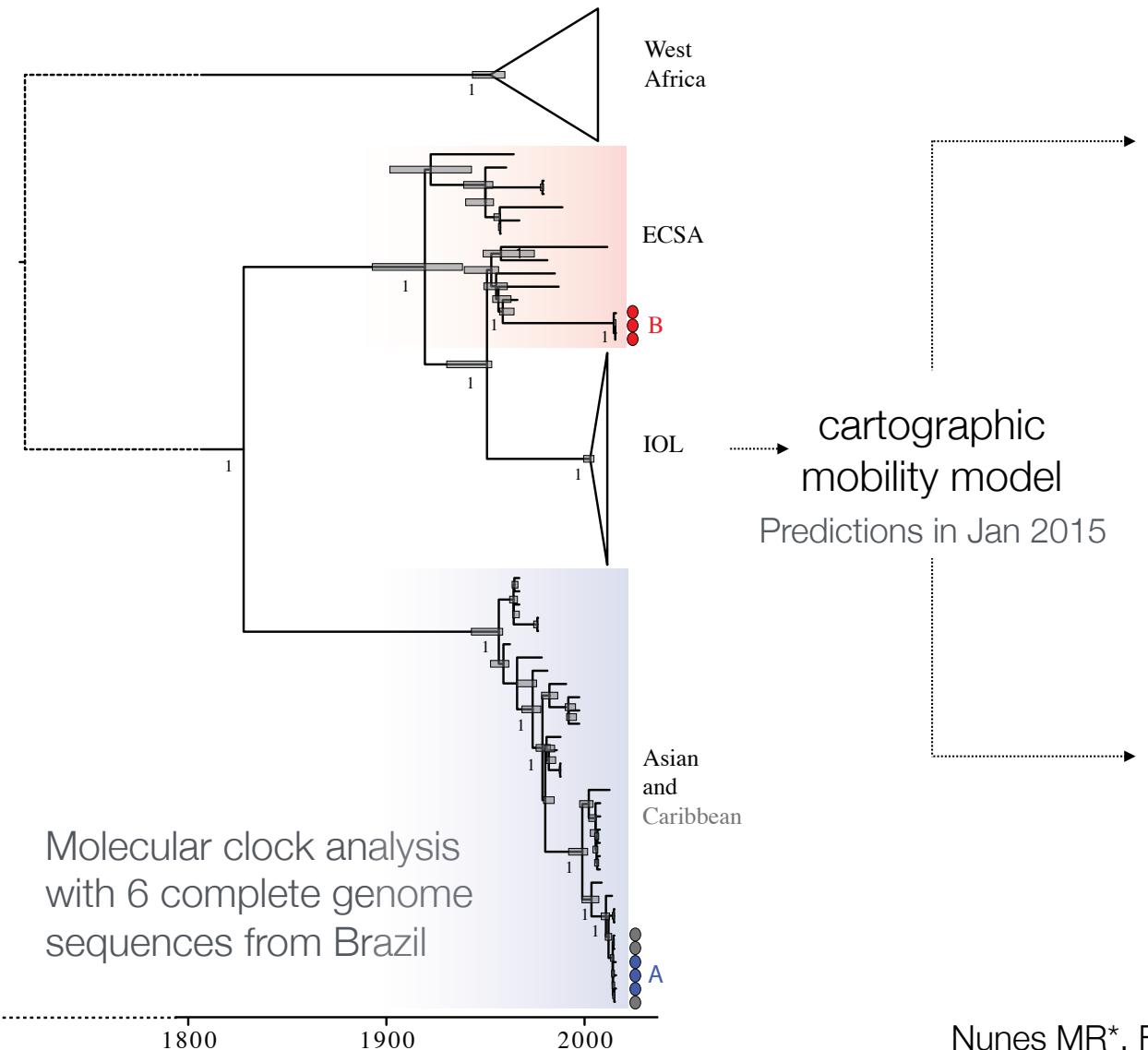
CHIKV-ECSA introduced in Brazil from Angola



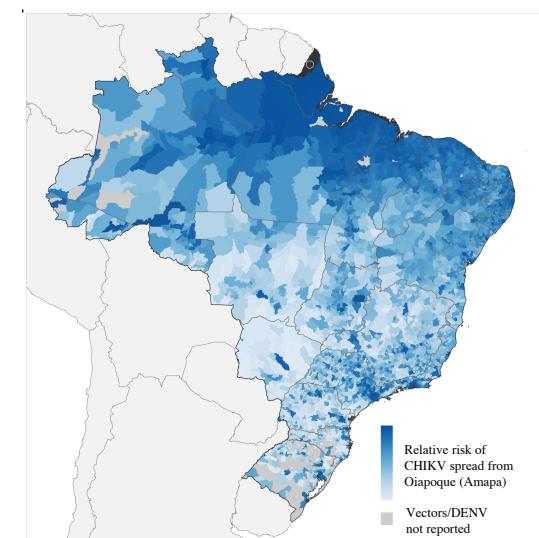
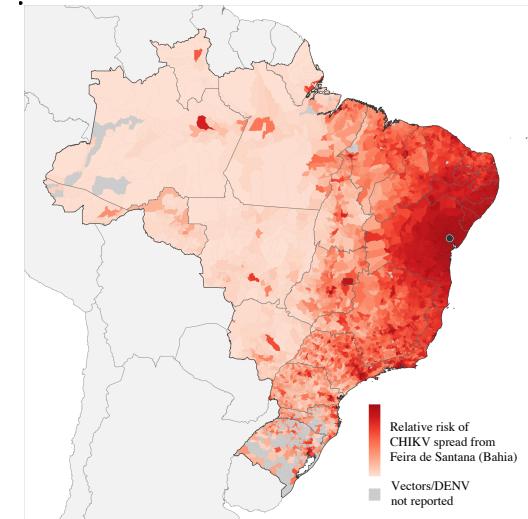
Feira de Santana, Bahia, Brazil, July 2014



Distinct CHIKV genotypes circulating in Brazil



Nunes MR*, Faria NR* et al. BMC Med, April 2015



CHIKV-ECSA genotype has been circulating in Northeast Brazil since mid-2014

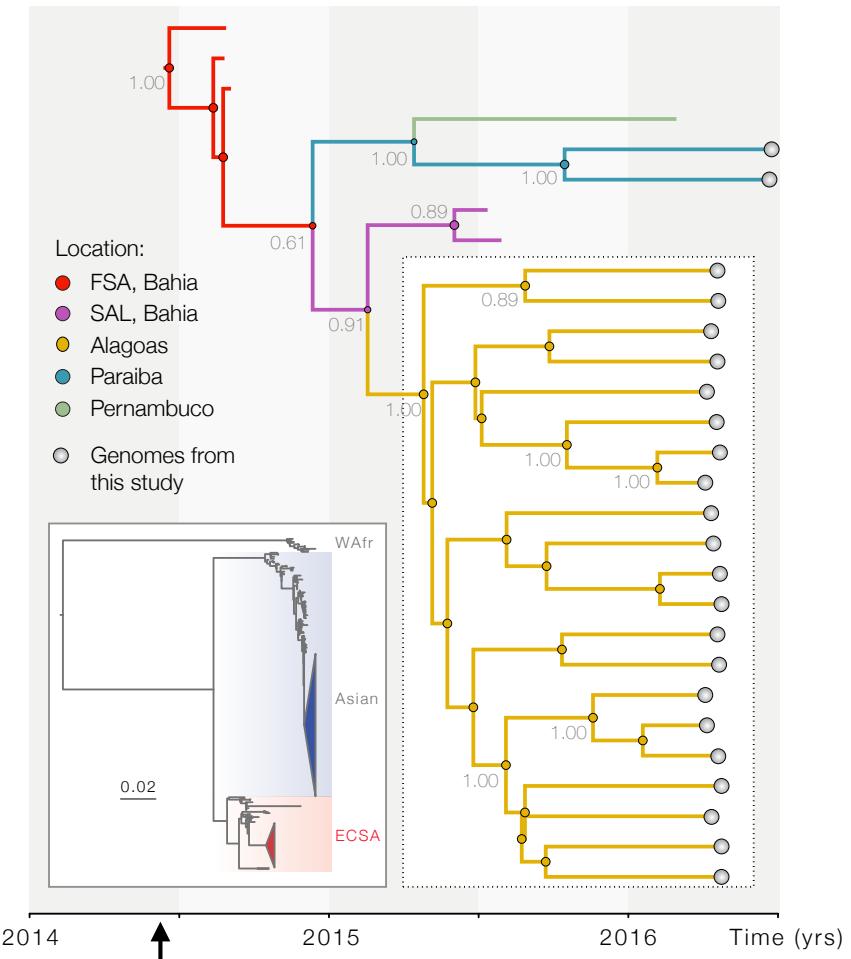
- 30 Mar - 3 May 2016, 12,000 visits in 2 hospitals in Maceió, Alagoas, Brazil
- 70% visits with exanthematous illness symptoms compatible with DENV, ZIKV or CHIKV
- 76% infected with CHIKV, 24% with ZIKV (RT-qPCR)
- 13% co-infected with CHIKV and ZIKV (RT-qPCR)
- fever (87%), arthralgia (70%), headache (44%), exanthema (30%) and myalgia (26%)

Two genotypes currently circulating in the Americas

CHIKV-ECSA genotype: *adaptive mutations associated with transmission in Ae. albopictus?*

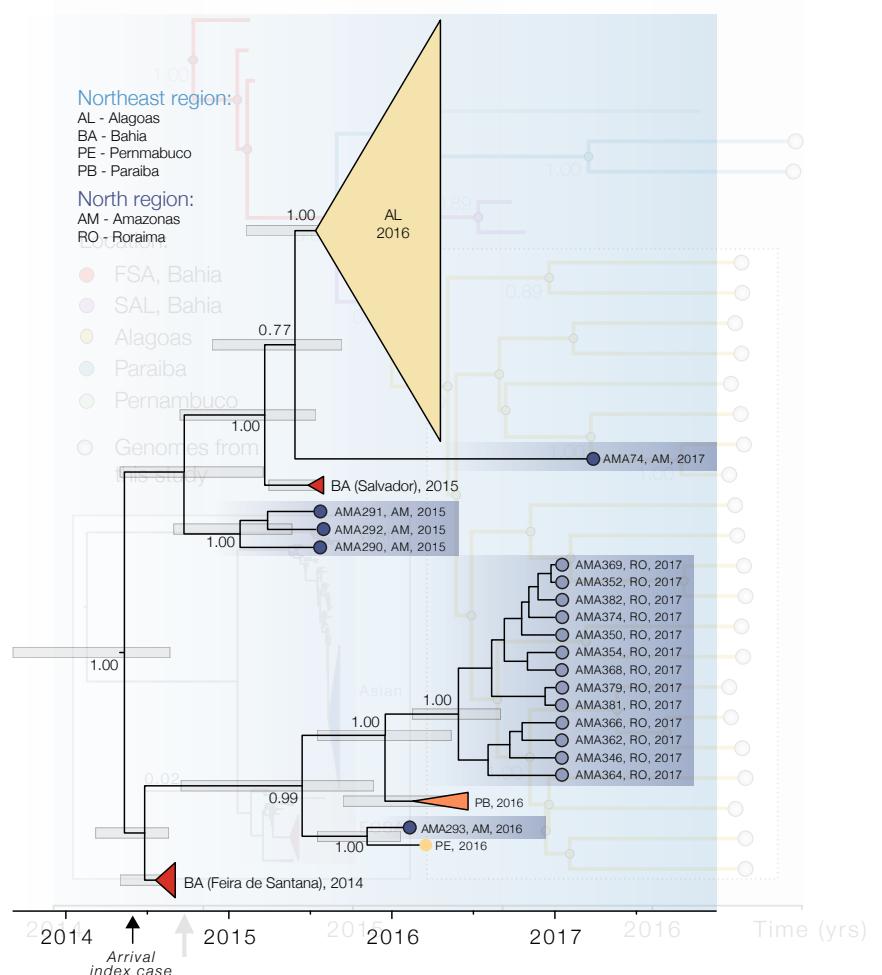
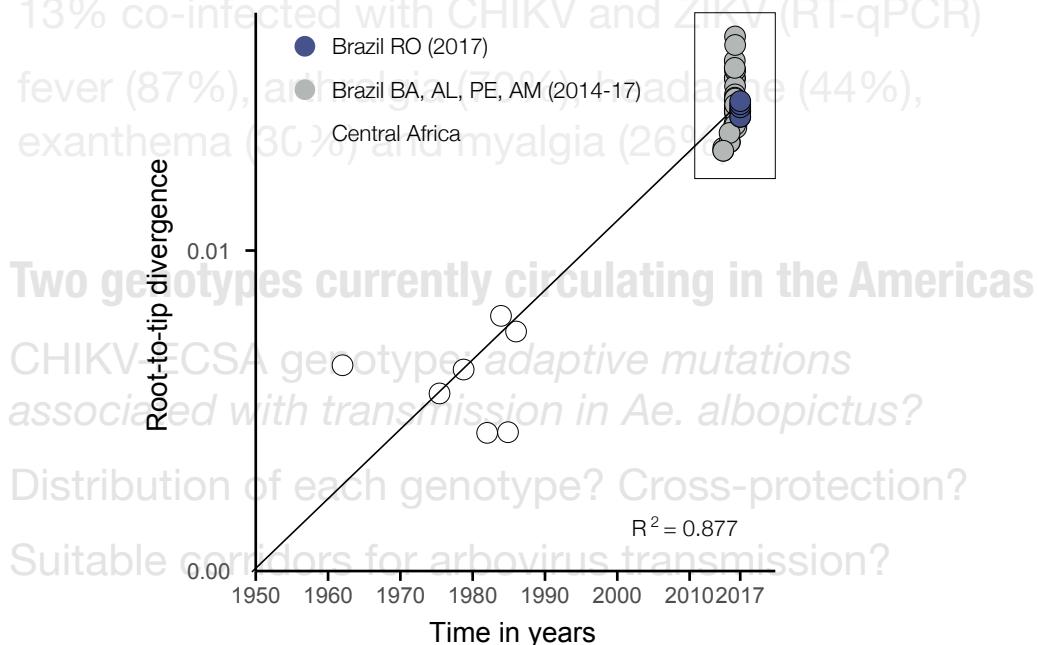
Distribution of each genotype? Cross-protection?

Suitable corridors for arbovirus transmission?

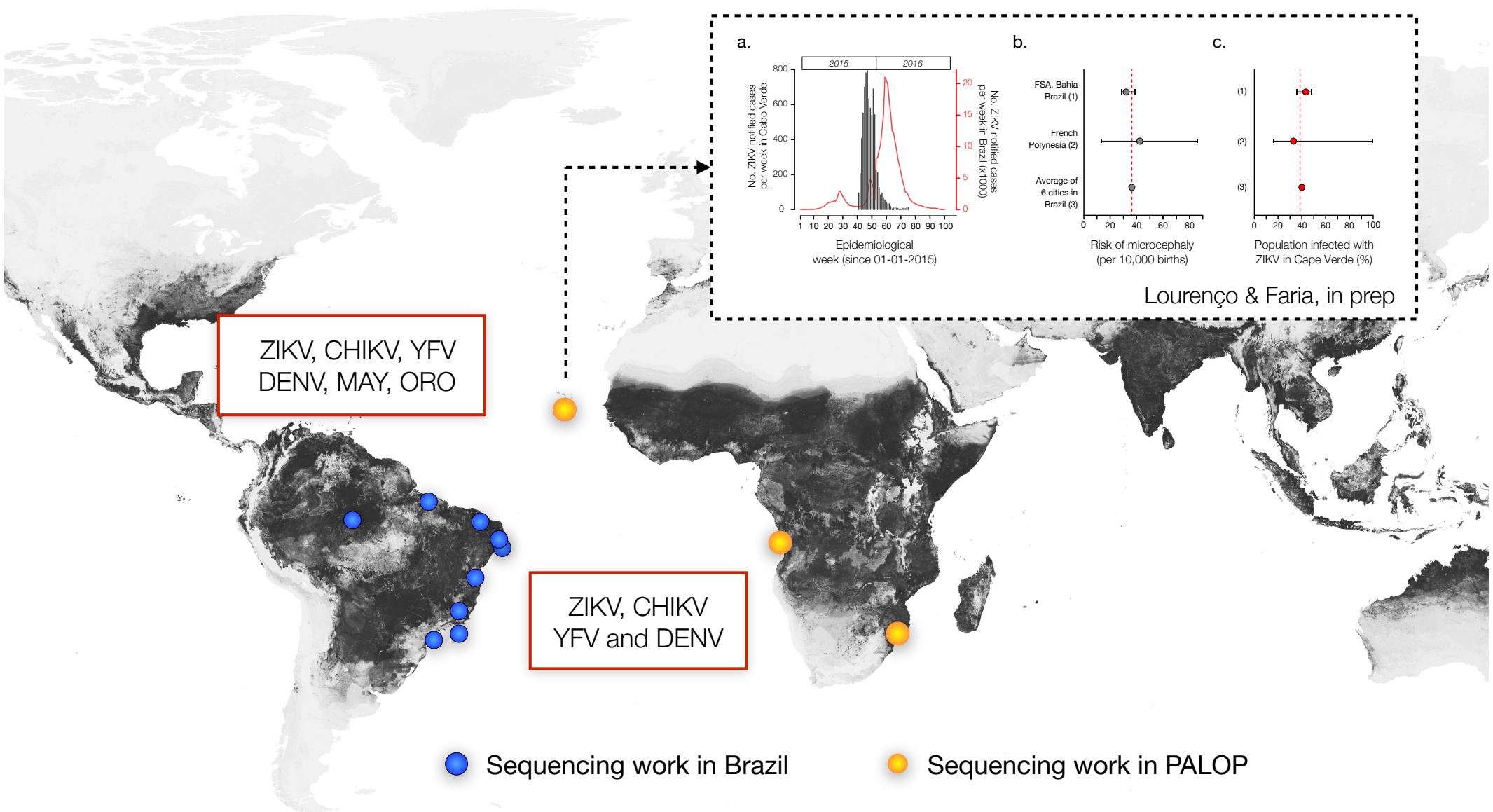


ZiBRA2 data ($n=18$): CHIKV-ECSA genotype in North Brazil since 2015

- 30 Mar - 3 May 2016, 12,000 visits in 2 hospitals in Maceió, Alagoas, Brazil
- Total of 62 ZIKV genomes and 18 CHIKV genomes generated in 7d
- 76% infected with CHIKV, 24% with ZIKV (RT-qPCR)
- 13% co-infected with CHIKV and ZIKV (RT-qPCR)
- fever (87%), arthralgia (70%), headache (44%), exanthema (30%) and myalgia (26%)



ArboSPREAD project: anticipating arbovirus spread across corridors of suitability



Acknowledgments (1)

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Jaqueline Goes de Jesus, LHGB/IGM/FIOCRUZ, Salvador, Bahia, Brazil

Antonio Charlys da Costa, University of Sao Paulo

Ingra Morales, University of Sao Paulo

Poliana da Silva Lemos, Instituto Evandro Chagas, Ministry of Health, Belém, Brazil

Luciano Franco, , Instituto Evandro Chagas, Ministry of Health, Belém, Brazil

Sandro Patroca, Instituto Evandro Chagas, Ministry of Health, Belém, Brazil

Trevor Bedford, Fred Hutchinson Cancer Research Center, United States

Bruna Nascimento, Instituto Evandro Chagas, Ministry of Health, Belém, Brazil

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Magliones (director of the LACEN Maceio)

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Rafael Freitas de Oliveira França, Department of Virology, FioCruz Recife

Constancia Ayres (coordinator of the Department of Entomology, FioCruz Recife)

Gabriel da Luz Wallau, Department of Entomology, FioCruz Recife

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