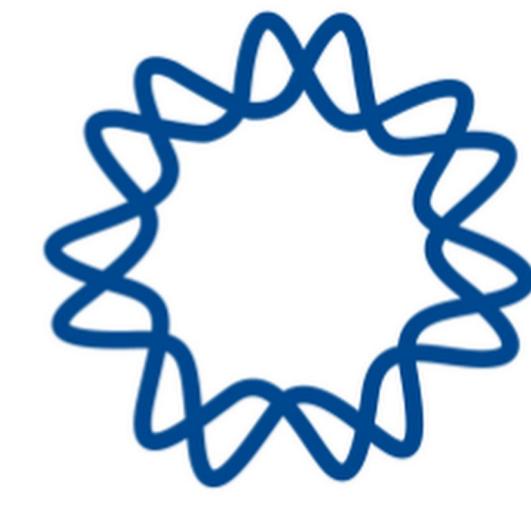


# Monitoring SARS-CoV-2 Coinfections Throughout Three Years Of The Covid-19 Pandemic In Mexico - Results From Covigen-Mex's Multi-Institutional Genomic Surveillance



Instituto de  
Biotecnología

Download poster:



Rodrigo García-López<sup>1\*</sup>, Blanca Taboada<sup>1</sup>, Selene Zárate<sup>2</sup>, José Esteban Muñoz-Medina<sup>3</sup>, Angel Gustavo Salas-Lais<sup>3</sup>, Alfredo Herrera-Estrella<sup>4</sup>, Nelly Selem Mojica<sup>5</sup>, Celia Boukadida<sup>6</sup>, Joel Armando Vazquez-Perez<sup>6</sup>, Bruno Gómez-Gil<sup>7</sup>, Alejandro Sanchez-Flores<sup>8</sup>, Carlos F. Arias<sup>1</sup>

<sup>1</sup> Departamento de Genética del Desarrollo y Fisiología Molecular, Instituto de Biotecnología, Universidad Nacional Autónoma de México, Cuernavaca, Mexico  
<sup>2</sup> Departamento de Genética del Desarrollo y Fisiología Molecular, Instituto de Biotecnología, Universidad Nacional Autónoma de México, Cuernavaca, Mexico  
<sup>3</sup> Coordinación de Calidad de Insumos y Laboratorios Especializados, Instituto Mexicano del Seguro Social, Mexico City, Mexico  
<sup>4</sup> Laboratorio Nacional de Genómica para la Biodiversidad-Unidad de Genómica Avanzada, Centro de Investigación y de Estudios Avanzados del IPN, Irapuato, Mexico  
<sup>5</sup> Centro de Ciencias Matemáticas, Universidad Nacional Autónoma de México, Morelia, Mexico  
<sup>6</sup> Centro de Investigación en Enfermedades Infectuosas, Instituto Nacional de Enfermedades Respiratorias Ismael Cosío Villegas, Mexico City, Mexico  
<sup>7</sup> Centro de Investigación en Alimentación y Desarrollo AC, Unidad Mazatlán, Mazatlán, Mexico  
<sup>8</sup> Unidad Universitaria de Secuenciación Masiva y Bioinformática, Instituto de Biotecnología, Universidad Nacional Autónoma de México, Cuernavaca, Mexico



\* Contact information:  
 Rodrigo García López, Ph.D.  
 rodrigo.garcia@ibt.unam.mx  
 @rodrigogarlop

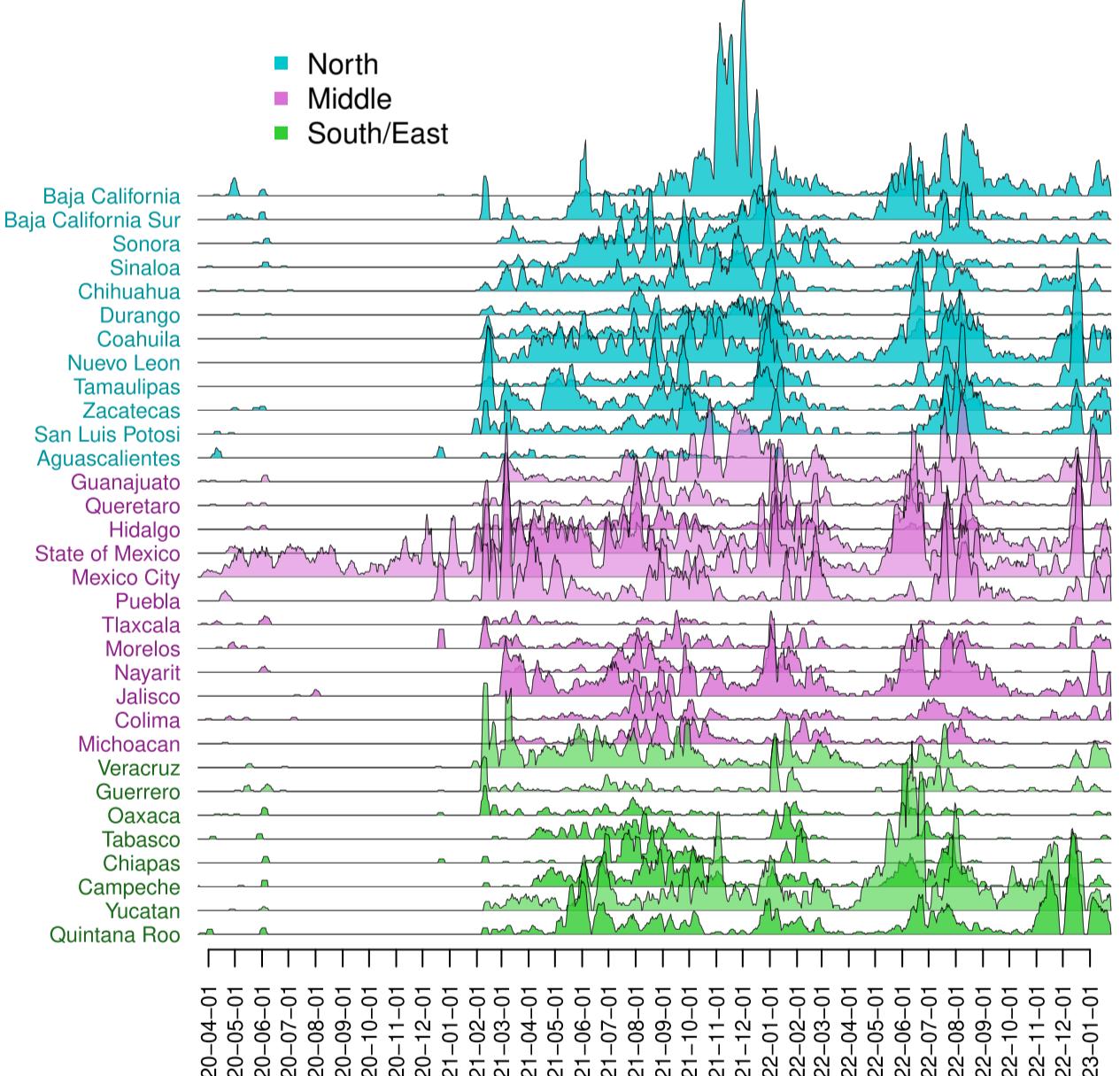
## Abstract:

The COVID-19 pandemic was marked by a succession of turnover events involving different relevant variants of the SARS-CoV-2 coronavirus that drove multiple epidemiological surges (waves). In Mexico, over the span of three years and six waves, the first nationwide dominant variant, B.1.1.519, was displaced by variants Alpha and Gamma, which were then superseded by Delta subvariants and later by multiple subvariants from the Omicron clade.

Periods of high transmission where at least two of these circulated fostered the occurrence of coinfections within patients, with variable ratios. In order to detect and study them, CoViGen-Mex, Mexico's largest genomic surveillance effort, set out to analyze collections of Intra-Patient Minor Allelic Variants (IPMAVs) in 29,661 public health samples collected from March 18, 2020 to January 27, 2023.

IPMAVs were defined as low-frequency allelic variants (<0.5) found in polymorphic loci of the SARS-CoV-2 genome that finely reflect mutational variation in the RNA molecules of different virions in a sample. Detection of full sets of variant-defining mutations as IPMAVs enabled the detection of putative low-frequency variants that coexisted as coinfections, for studying their longitudinal and geographical distribution as they prove an important step for the evolutionary process of the virus that may favor recombination.

**Our Dataset:**  
 Nasopharyngeal samples from 32 States in Mexico:

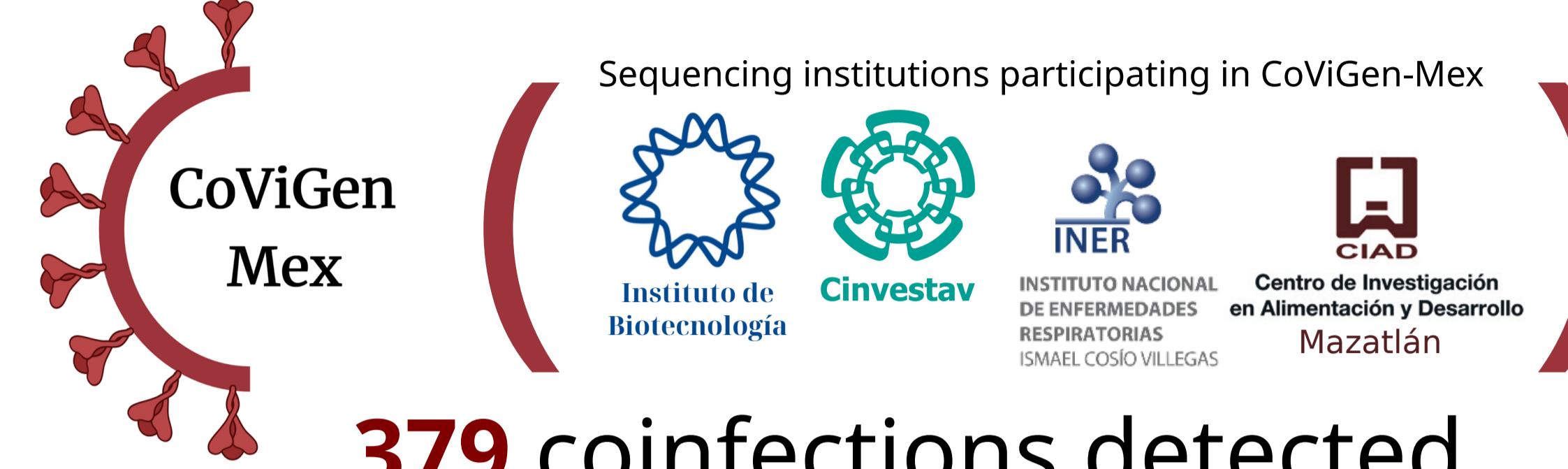


~1/3 of all Mexican samples.  
 The largest collection of samples outside Mexico City and its suburbs.

3 years worth of SARS-CoV-2 sequencing data.

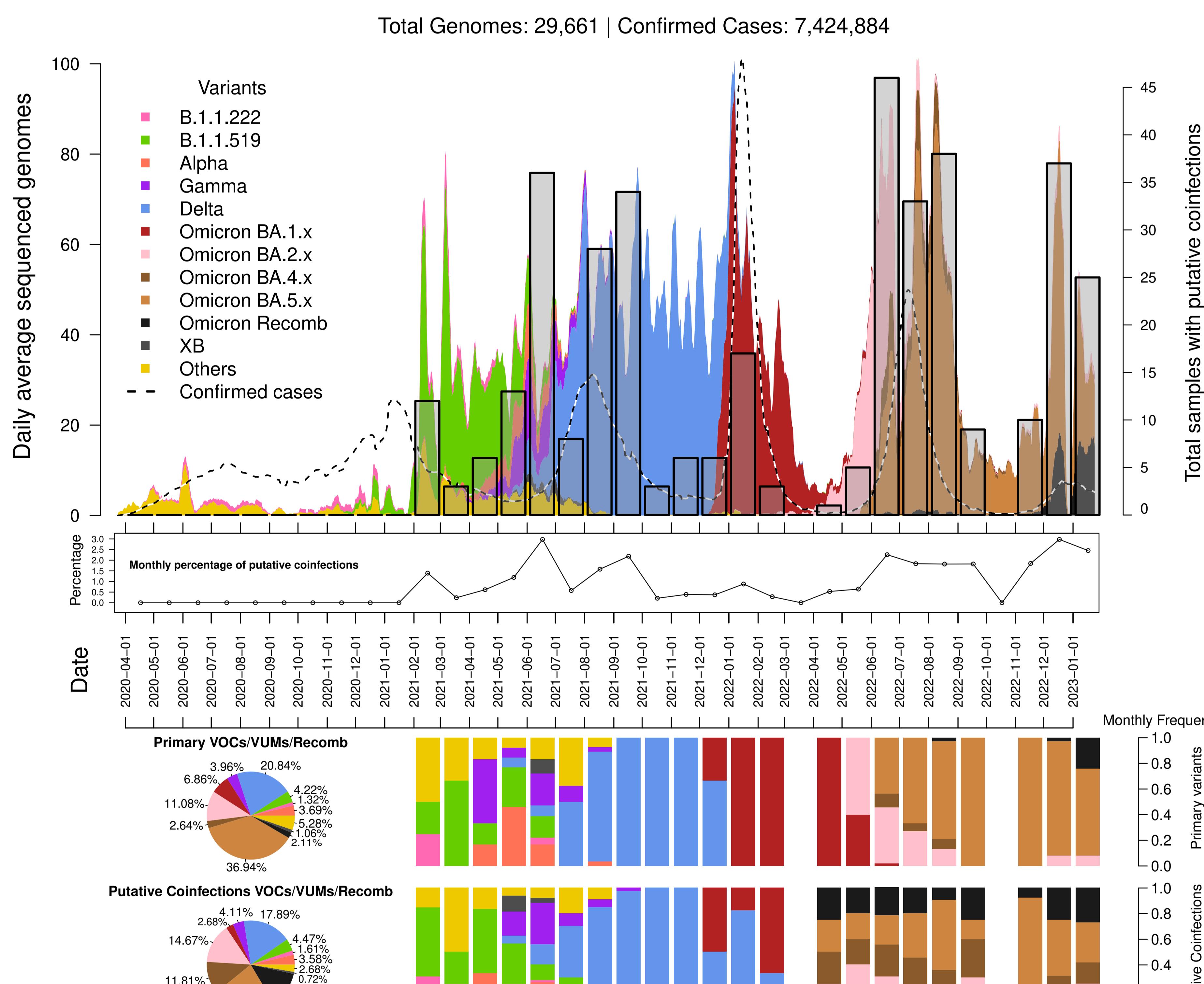


29,661 SARS-CoV-2 sequenced genomes



379 coinfections detected

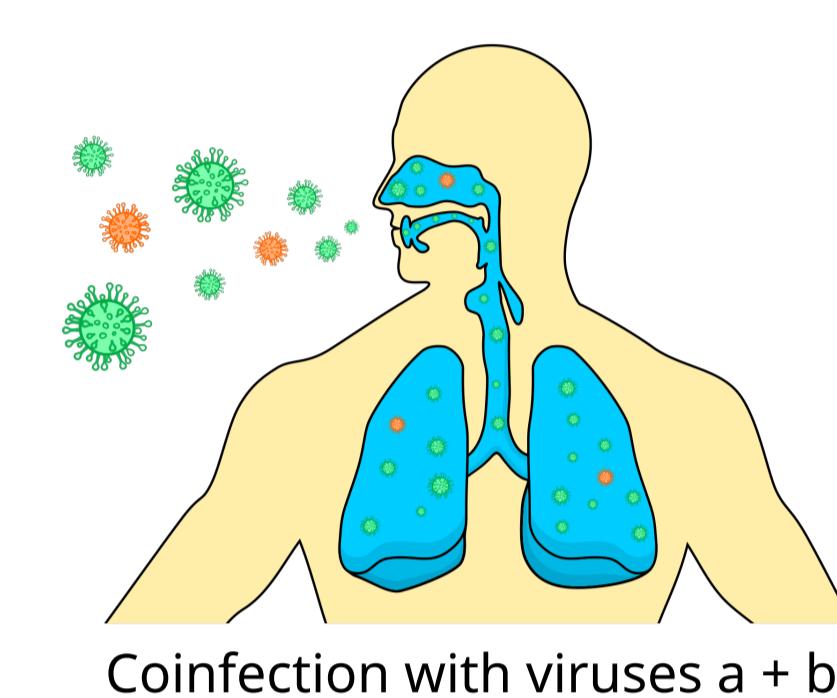
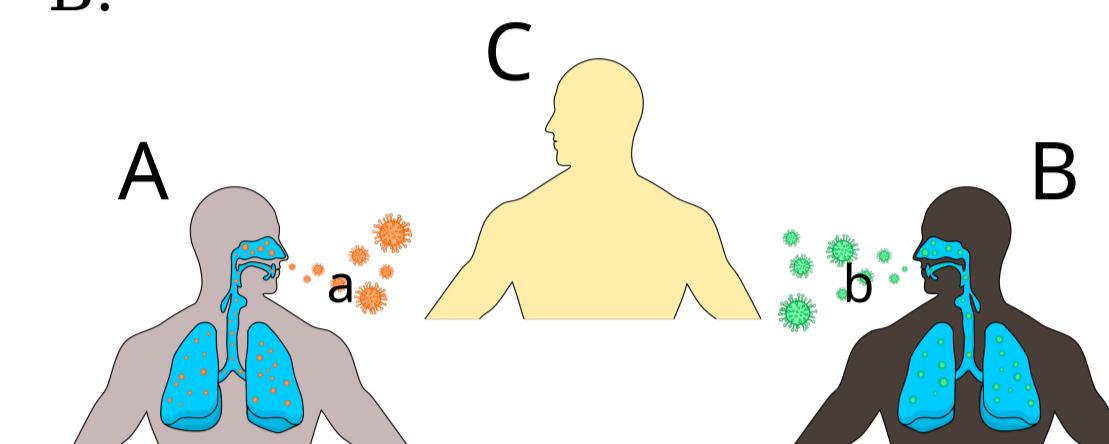
**! Main finding:**  
 Mixed mutation profiles from multi-variant SARS-CoV-2 coinfections were relatively common in sequences from Mexican samples, occurring at a rate of 1.28% but varied monthly, ranging from 0.21% to 2.98%



## Origin of most coinfections:

When multiple variants coexist in a population at the same time, chances increase of getting infected by multiple variants.

Example: Patient C is exposed to different SARS-CoV-2 variants (a and b) carried by patients A and B.



Coinfection with viruses a + b  
 Both variants compete within patient C but one of them is dominant (70-90% of sequenced genomic fragments).

Variant Mutation profile  
 a: b:

Viral variants carry a different set of mutations that may be used to identify them in a sample.

## Result's highlights:

SARS-CoV-2 coinfections can be detected bioinformatically from genomic datasets from COVID-19 positive samples.

Second generation high-throughput sequencing platforms are required (e.g. Illumina's SBS).

Studying low-frequency allelic variants (IPMAVs) is mandatory.

In Mexico:

- ~1 in every 78 samples had a secondary variant (normally one).

- Secondary variants are found in a ratio of 1:3 or less (avg: 23%).

Coinfection distribution was strongly dependent on the sequencing effort and the total variants that co-occur in each period.

- The two periods with more coinfections were 1) Onset of early VOCs (prior to Delta and 3rd wave) and 2) Diversification of Omicron BA.2 (wave 5).

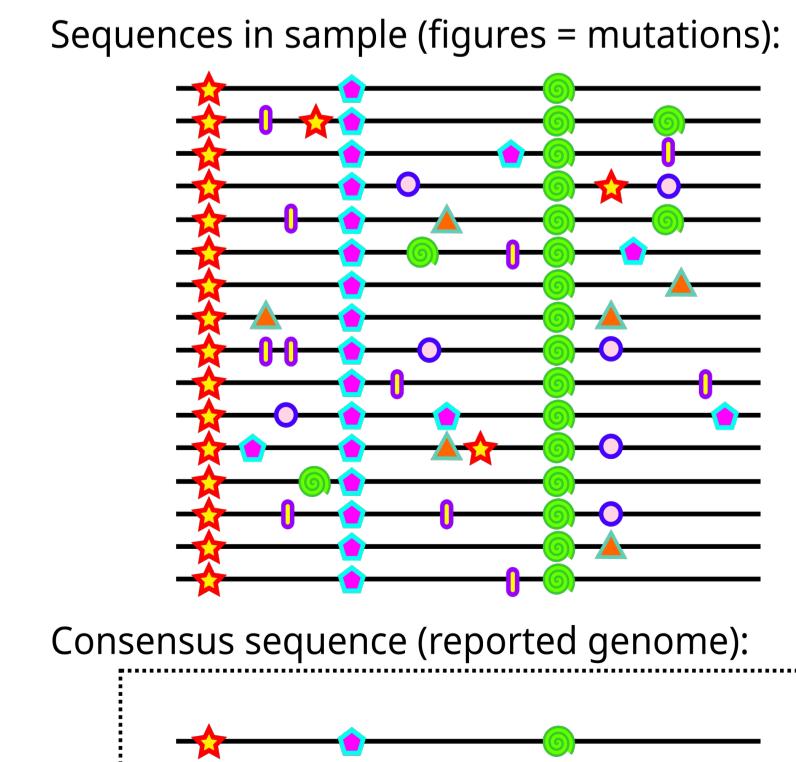
No statistical significance was found for disease severity, geographic location, sex nor age.

## ! Main Focus of the Study:

Intra-Patient Minor Allelic Variants (IPMAVs), mutations that are not part of the consensus sequence

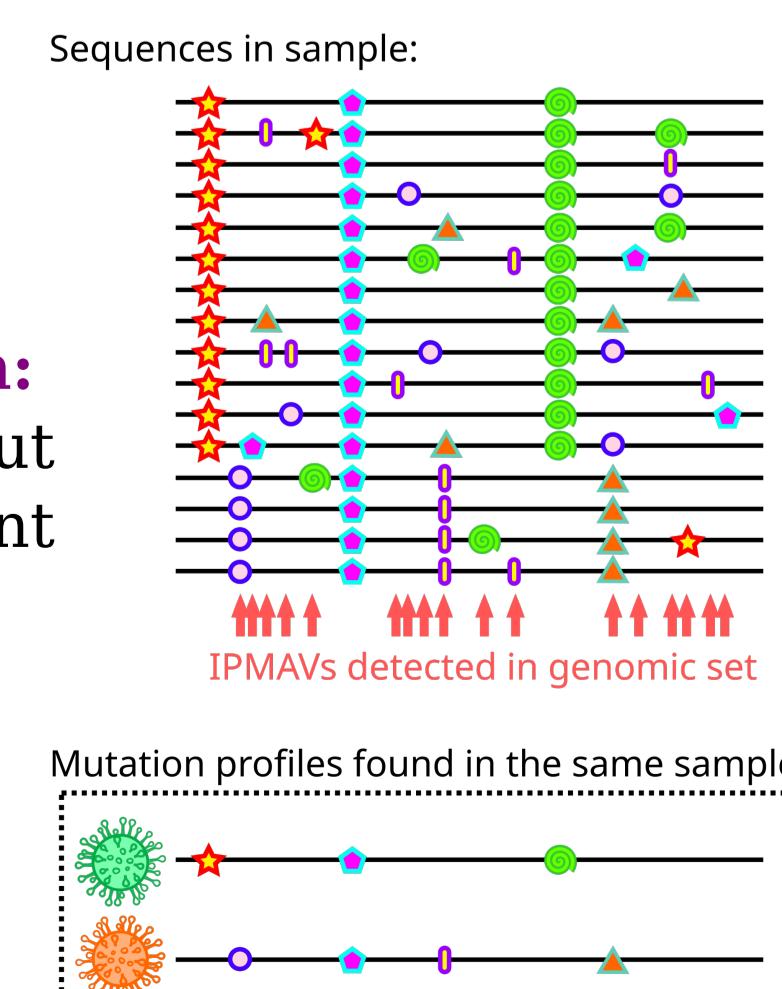
**"Genomes"** are consensus sequences:  
 Most COVID-19 studies report a single viral genome per sample, but each of those sequences is in fact a consensus constructed from multiple sequencing reads.

Fixed mutations occur in most reads of the same loci.



**IPMAVs provide valuable information:**  
 Not just inner patient variation, but coinfections occurring within a patient are commonly ignored.

IPMAVs occur with allelic frequency <0.5%



## An example of one of 379 coinfections:

Two profiles were found in a female patient from Baja California. The consensus sequence was determined as Gamma variant. The secondary variant was determined as Alpha. Both had complete mutation profiles.

