Building Genomic Epidemiology capacity for epidemic preparedness and response in Africa, the Mali University Clinical Research Center experience

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Introduction to Genomic Epidemiology

- **Definition and Importance**:
  - Genomic epidemiology involves the study of pathogen genomes in relation to associated metadata.
  - It is crucial for monitoring disease dynamics and tracking the emergence of new variants.
- **Role in Public Health**:
  - Helps understand the spread and evolution of infectious diseases.
  - Provides data to inform public health responses and strategies.
- **Technological Advances**:
  - Recent advances in sequencing technologies have made genomic epidemiology more accessible and powerful.
  - Techniques such as metagenomic and targeted sequencing allow for the detection and characterization of a wide range of pathogens.
- **Application in Africa**:
  - Africa faces unique challenges with infectious diseases due to limited resources and a high burden of morbidity.
  - The implementation of genomic epidemiology can significantly improve surveillance and disease response capacities across the continent.

University Clinical Research Center (UCRC)

- The UCRC is an initiative between the Ministry of Health of Mali, the Ministry of Higher Education, the University of Sciences, Techniques, and Technologies of Bamako (USTTB), and the NIAID/NIH.

- The collaboration aims to facilitate clinical research in Mali.

- First biosafety level 3 laboratory in the country.

- Provides basic and personnel research capacities for scientific research, clinical research, data management, bioinformatics, diagnostic methods (with an immuno-core, a molecular biology and genomics laboratory, and biosafety level 3).

- The first cases of Ebola and COVID-19 were diagnosed at the UCRC.

Director: Pr Seydou Doumbia

Technological Platforms of the UCRC

- **Sanger Sequencing:**
  - Traditional method with high precision for specific targets.
  - Often used for validation and confirmation of results.

- **Oxford Nanopore Technologies (ONT)**
  - Offers portable and real-time sequencing capabilities.
  - Suitable for rapid, field-based response scenarios.

- **Illumina:**
  - Provides high-throughput sequencing with great precision.
  - Ideal for comprehensive genomic studies.

- **Integration with Routine Diagnostics for Surveillance:**
  - Genomic techniques are integrated into routine diagnostic methods such as rapid diagnostic tests (RDTs), RT-PCR, and ELISA.
  - • This integration provides a robust platform for pathogen detection and characterization.

- **High-Performance Computing(HPC) Server**
  - For bioinformatic analyses

ABI 3500 Genetic Analyser

ONT MinIon Mk1C

NextSeq 1000 Sequencing Systems

Capacity Building and Collaboration

- The UCRC leverages genomic, and bioinformatics capacities built in collaboration with the National Institute of Allergy and Infectious Diseases (NIAID) and Columbia University.

- Establishes nationwide genomic detection capabilities in Mali.

- Strengthens preparedness and response capacities for sub-regional epidemics.

- Provides training and resources to local health scientists and professionals (training grants, training in data sciences, bioinformatics, etc.).

Unexplained Fever patients , using virome capture metagenomic sequencing

- ## VirCapSeq-VERT
  - Metagenomic sequencing platform designed to capture and sequence viral genomes from clinical samples..

- ## Detection of Pathogens
  - Pathogens were detected in 79.6% of cases.
  - Measles, Plasmodium spp., Salmonella spp., and SARS-CoV-2 were among the detected pathogens.
  - The identification of more than one concurrent pathogen was common (41.5%)

Integrating metagenomic sequencing with routine laboratory diagnostic testing enhances the detection of pathogens in acute febrile illnesses, highlighting its potential value in identifying infectious etiologies in resource-limited settings
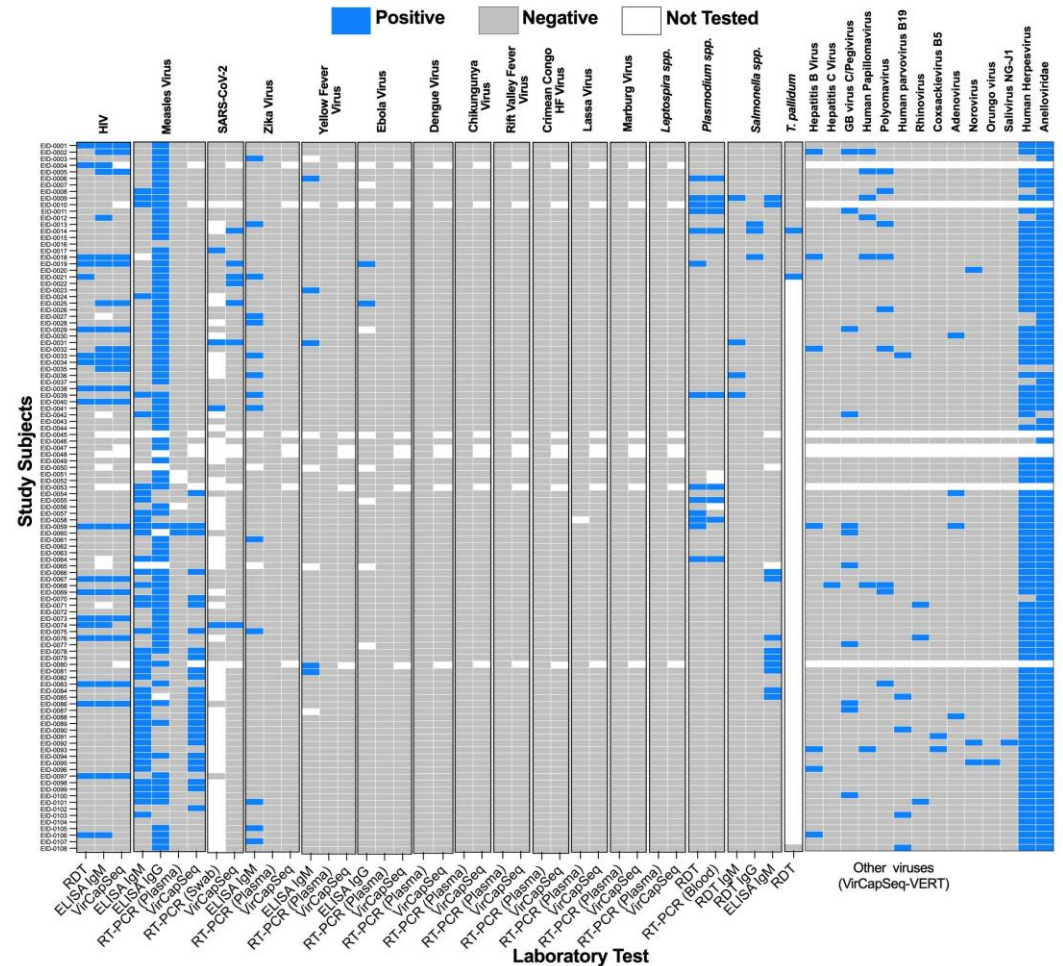
All laboratory test results from baseline samples for each subject in the ECERID study. Additional pathogens identified by VirCapSeq-VERT are shown in the rightmost group of columns.

Paper accepted for publication (AJTMH,2024)

COVID-19 Surveillance (Identification of SARS-CoV-2 Variants)

- **Detection of SARS-CoV-2 Variants**:
  - Genomic surveillance during the COVID-19 waves identified **seven distinct SARS-CoV-2 variants** in Mali.
  - Delta, Alpha, Beta, Eta, and 20A.

- **Importance of Continuous Surveillance**:
  - Continuous surveillance is essential to track the emergence and spread of new variants.

Koné, Amadou et al. "Dynamics of SARS-CoV-2 variants characterized during different COVID-19 waves in Mali."
IJID regions vol. 6 (2023): 24-28.
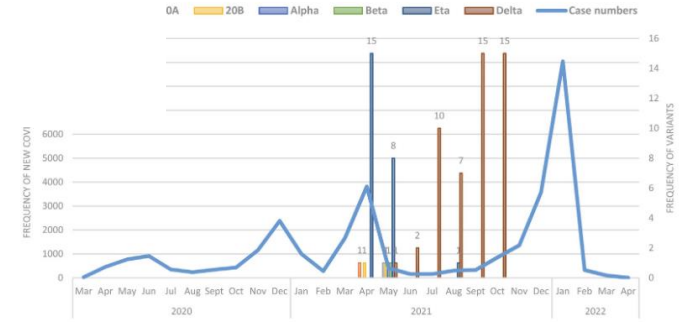doi:10.1016/j.ijregi.2022.11.009
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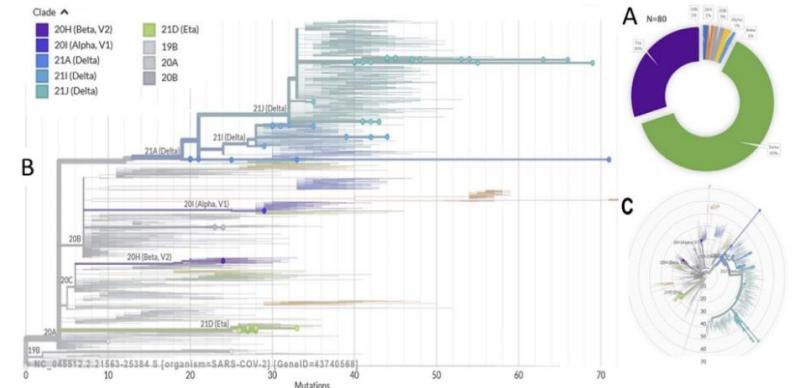
2023 Dengue Virus Epidemic

- **Genomic Sequencing of Dengue Virus**:
 - Sequencing efforts during the 2023 epidemic identified **serotype 3** of the dengue virus (DENV-3) as the predominant strain.
  - Provides critical information on the spread of the virus and co-infections.

- **Impact on Public Health**:
  - Informs public health responses and interventions to control the epidemic.
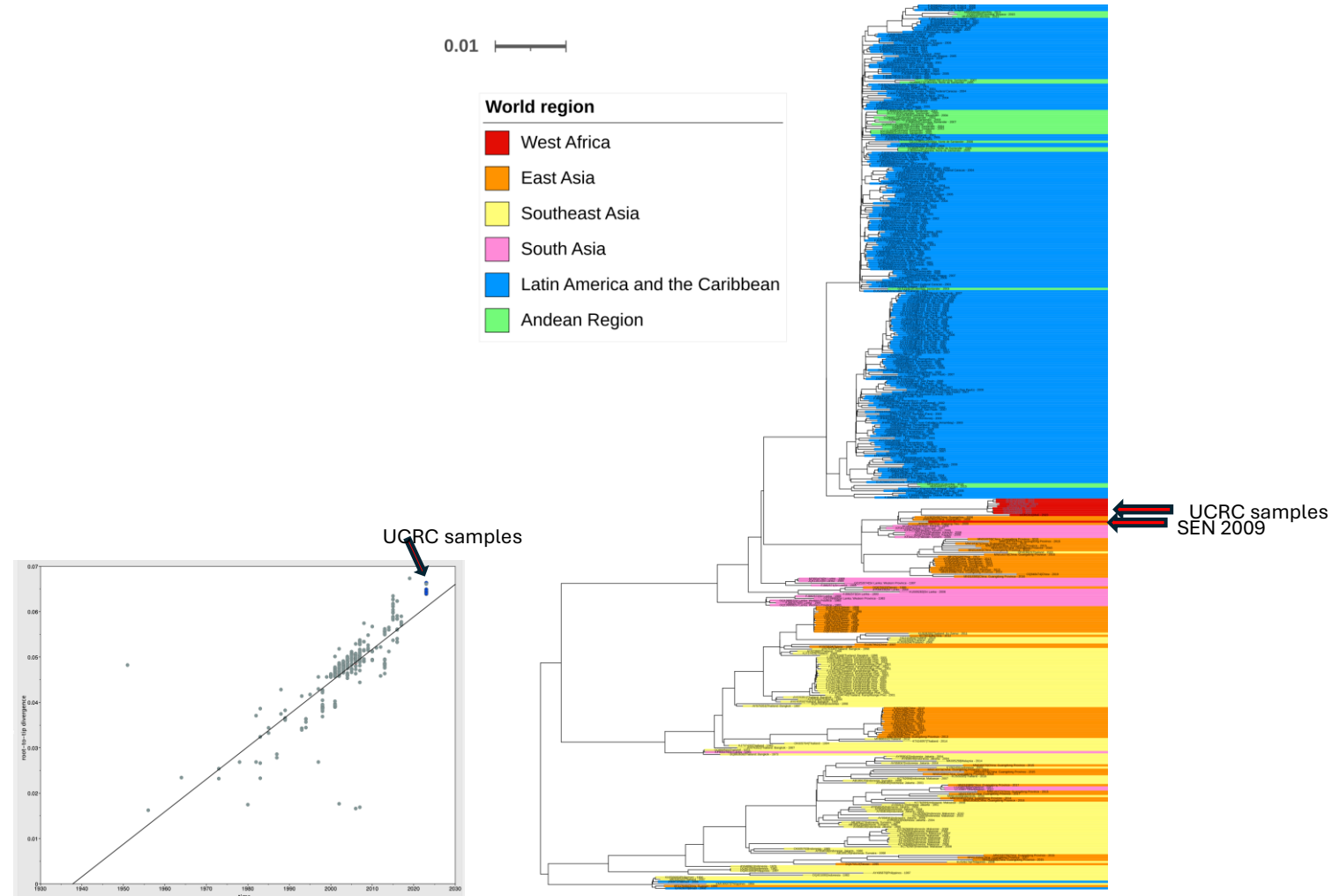
DENV3 Time-calibrated phylogenetic trees

Measles Virus Genomic Surveillance in Mali

- Using VirCapSeq-VERT, a metagenomic sequencing tool, **23 near-complete measles virus genomes** were sequenced from samples collected across Mali between 2012 and 2022.

- The study identified **genotype B3.1** as the predominant strain circulating in Mali, consistent with regional transmission patterns across West and Central Africa.

- One case was linked to vaccine-associated rash illness (VARI), highlighting the method's broad detection capability.

- This research fills a gap in whole-genome sequencing data for measles in West Africa and emphasizes the importance of genomic tracking for outbreak management.
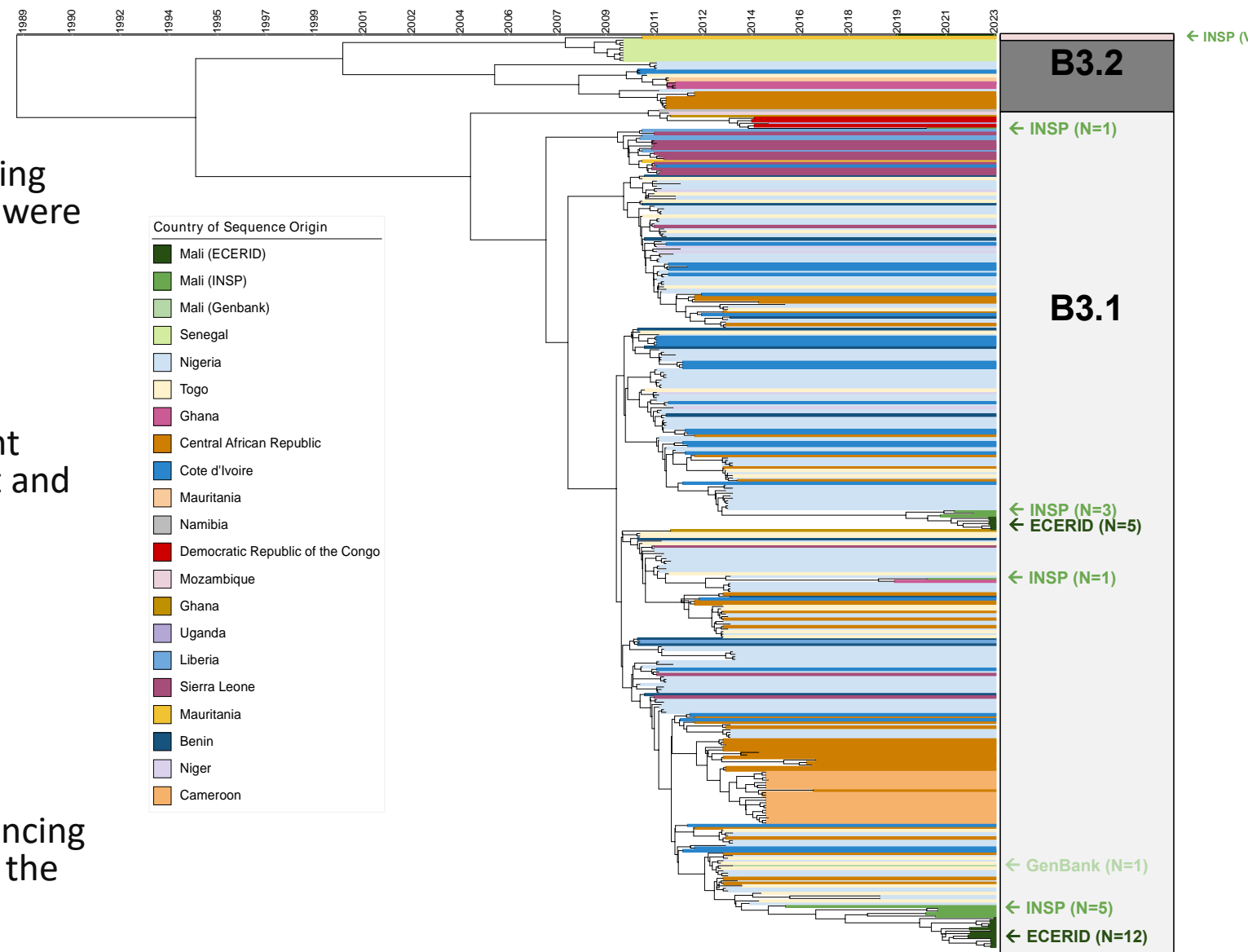
Phylogenetic tree of measles B3 genotype nucleoprotein sequences from West and Central Africa , generated by Bayesian Markov chain Monte Carlo method.

Already submitted for publication

Key Lessons

- **Improved Pathogen Detection**:
  - Genomic approaches significantly enhance pathogen detection compared to conventional methods alone.

- **Real-Time Surveillance**:
  - Real-time genomic surveillance is crucial for monitoring emerging variants and guiding timely public health responses.

- **Capacity Building**:
  - Strengthening local capacity in genomic sequencing is essential for sustainable epidemic preparedness.

- **Collaborative Efforts**:
  - Collaboration between local and international partners combines resources and expertise to effectively tackle global health challenges.

Conclusion

- **Model for Resource-Limited Settings**:
  - The UCRC's genomic surveillance program serves as a model for integrating advanced genomic tools into epidemiological research and public health practice in resource-limited settings.

- • **Future Directions**:
  - Ongoing efforts to improve genomic surveillance and capacity building.
  - Continued collaborations to address emerging infectious disease threats.

Acknowledgments

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