GINKGO BIOWORKS | concentric by GINKGO

Aircraft wastewater pathogen monitoring across the world

International Conference towards a Global Wastewater Surveillance System for Public Health

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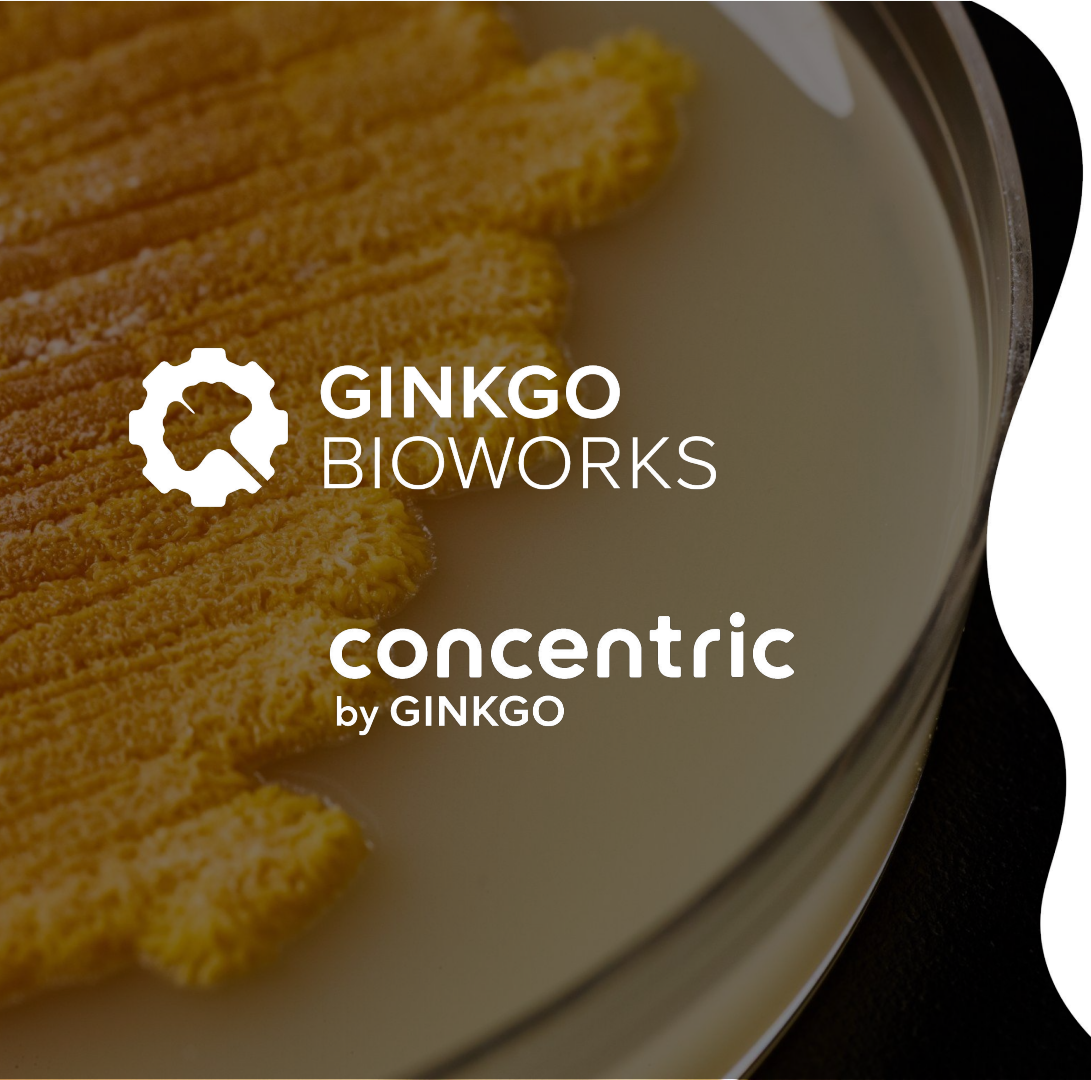
15-17 November, 2023



Building a horizontal platform for cell programming and biosecurity

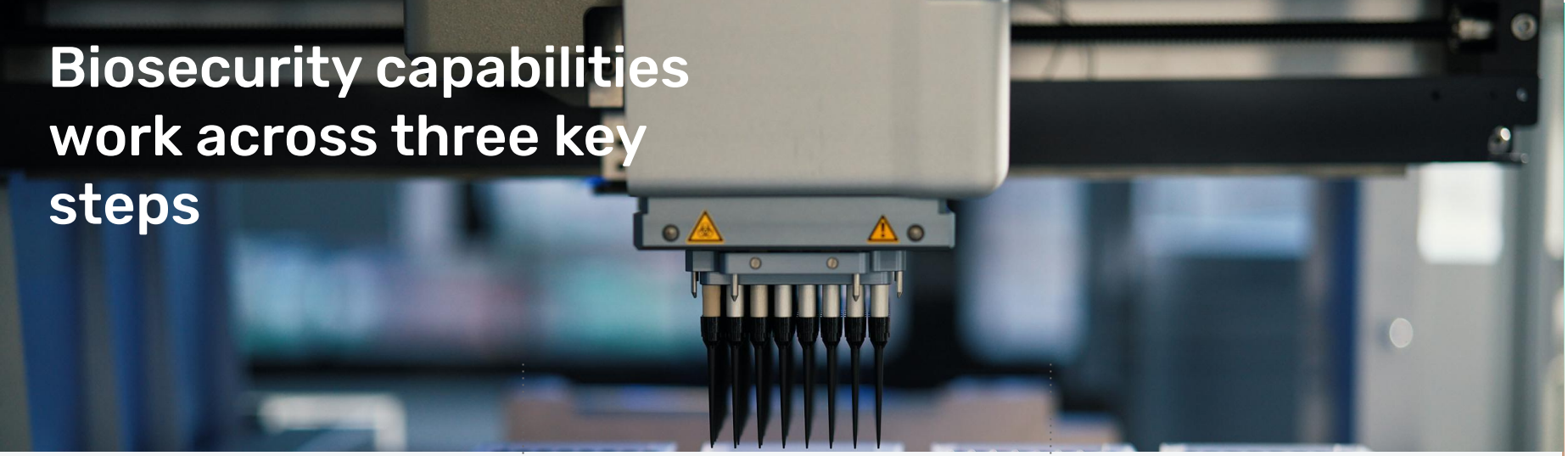
Founded in **2008** *to make biology easier to engineer*

Headquartered in **Boston**

Cell engineering foundry that engineers millions of organisms per year, with **3.8 billion gene sequences** to date

Ginkgo's **global biosecurity capability** includes non-traditional collection, end-to-end lab services, and bioinformatics, associated with over **12.5M samples and over 65K sequences since 2020**

Biosecurity capabilities work across three key steps



Monitor	Analyze & Inform	Prevent & Respond
Bioradar - Globally Distributed Surveillance	**Threat Identification Technology & Protocols**	**Rapid Response & Recovery**
Monitoring for new threats, through **active and passive monitoring capabilities**	Leverage data to **recognize threats before they spread**	**Help prevent or mitigate pathogen threats**, minimize effects, and recovery

Airports can serve as critical nodes for pathogen detection

- Travelers are an important population to consider when **tracking new and emerging infectious diseases,** acting as sentinels to identify transmission and spread.
- Collecting samples and using pathogen genomics enables to:
    - **Fill gaps in global surveillance** by providing data about geographies with limited pathogen monitoring or reporting.
    - **Enhance early detection** of new pathogens and variants weeks before they spread among communities
- Better information and faster detection can **improve health outcomes** and **reduce economic impact.**

Risk scoring and network analysis to design an idealized network for early biothreat detection

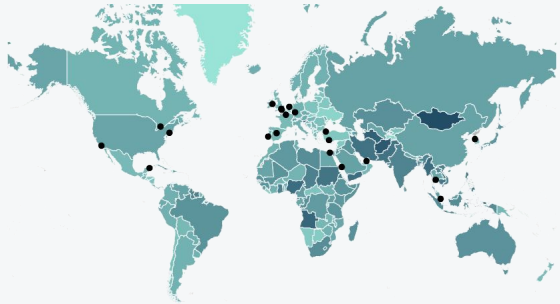
Methods

- Determine risk scoring factors relevant to the emergence of a new unreported outbreak
- Calculate country risk scores; determine which have highest scores (“country of interest”)
- Use travel data to identify travel hubs with optimal coverage of countries of interest
- Quantify early detection value of network vs. status quo

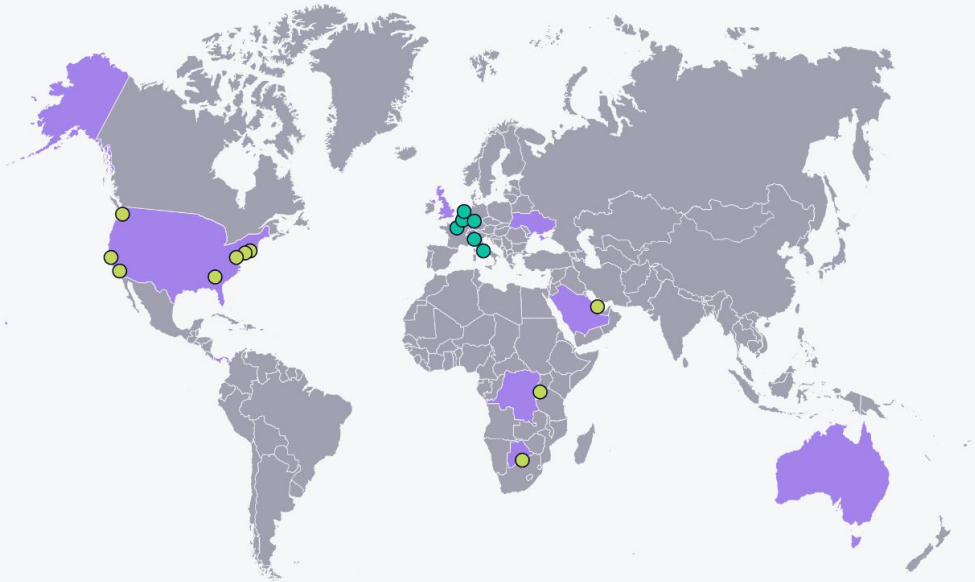
Example Scoring Factors	
Presence of Biological Research	Under-reporting
Conflict and Political Stability	Connectivity Patterns
Geographic Spillover Risk and Population Size	Public Health Surveillance Capacity

Output

- Model has identified **20 key hubs** providing optimal coverage of countries of interest to enable more rapid detection of outbreaks and novel pathogens
- **Next step:** Quantify time-to-detection of network vs. status quo



Working with local partners to support the activation of airport-based programs



Countries in which Concentric has active programs, pilots, or MoUs

Airport locations

Data analysis support for EU airport location

*Map is not exhaustive; some partnerships remain confidential.

Data updated 11/01/23

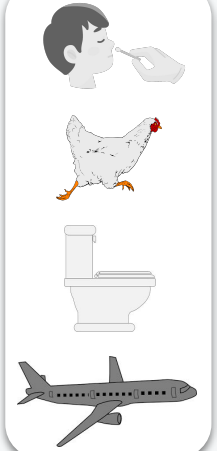
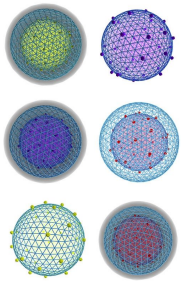
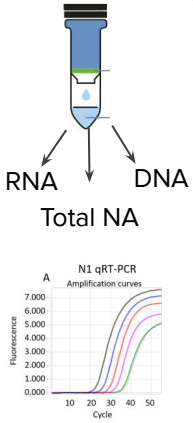
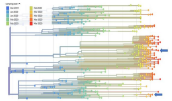
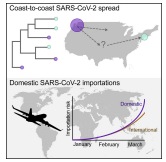
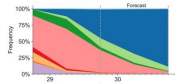
9
operational airport programs

6
Data analysis support for EU airport location

14
Countries with active programs, pilots, or MOUs (plus multilateral partnerships with Africa CDC and African Risk Capacity)

105
Countries of origin of flights sampled, across 6 continents

Each node leverages Next-Generation Pathogen Genomic capabilities

MONITOR/ COLLECT	PROCESS/ ENRICH	EXTRACT/ SCREEN	SEQUENCING PREP	SEQUENCE	ANALYZE	ALERT	FORECAST
	 CERES NANO	 RNA DNA Total NA	**Capabilities** RT-qPCR & ddPCR Amplicon (SARS-CoV-2) Whole Genome Seq  **Pre-capabilities** Probe Enrichment (RPIP) *Human read depletion* *Bacterial rRNA depletion* *Environmental Seq & Metagenomics* *RNA-seq*	**Instruments in-house** Illumina MiSeq Illumina NextSeq Illumina NovaSeq Nanopore MinION Nanopore GridION Nanopore PromethION PacBio Sequel II 	**Capabilities** Consensus genome Variant calling Deconvolution Characterization  GISAID GitLab AWS | S3 nf-core	 	**Capabilities** Risk assessment Immune escape Transmissibility  

Genomic Surveillance: Wet-lab

- **Direct metagenomic sequencing:** broad agnostic detection
- **Amplicon based:** targeted, specific and sensitive PCR-based amplification
- **Enrichment panels:** flexible probes for a well-defined but broad array of targets

Genomic Surveillance: Bioinformatics

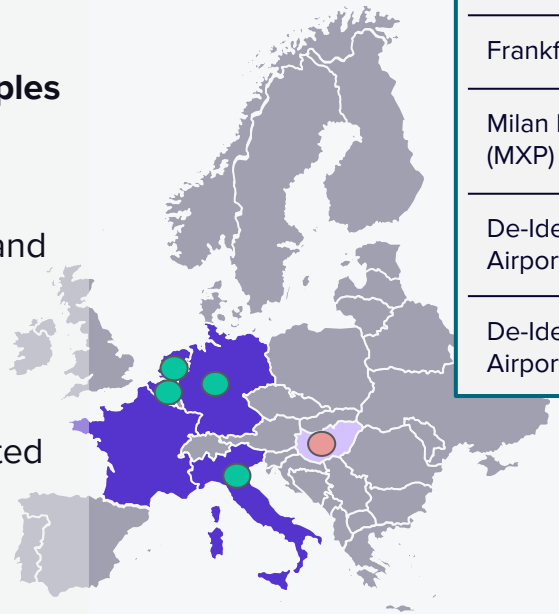
- **Mapping & variant calling:** generate consensus genomes
- **Lineage assignment and Phylogenies:** call lineages and find ancestors
- **Deconvolution:** identify frequency of multiple lineages in complex samples
- **Bespoke characterization:** characterize sample composition
- **Workflow management:** sharable & reproducible community driven pipelines

The Joint Research Center (JRC), Ginkgo, and EU Partners are conducting a pilot of what a European network might look like

Objective: Conduct **simultaneous sampling** at airport locations **across Europe** and compare results.

Approach: Worked with JRC to set up sample collection at **6 EU airports.**

- **Pilot partners** provided **23 wastewater samples** over 2 weeks from **aircraft (6) and airport sewage (17)**
- Samples underwent extraction, PCR testing and WGS at the **Hungarian National Center for Public Health and Pharmacy (NNGYK)**
- We analyzed sequencing data using **Ginkgo's bioinformatics pipeline**, and reported **results to participating countries.**

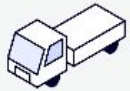


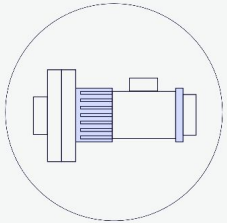
Airport	Sampling Location/Modality
Schiphol (AMS)	Airport wastewater
Brussels (BRU)	Airport wastewater
Frankfurt (FRA)	Airport wastewater
Milan Malpensa (MXP)	Airport wastewater
De-Identified Airport, France	Airport wastewater
De-Identified Airport, Italy	Aircraft wastewater

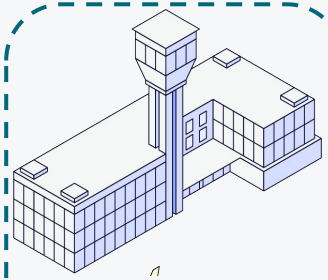
NNGYK NATIONAL CENTER FOR PUBLIC HEALTH AND PHARMACY

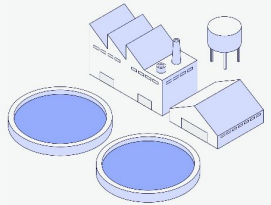
For this exercise, we have focused on 3 sampling modalities: Aircraft wastewater, terminal wastewater, and airport treatment plants

More granular ⟷ Less granular



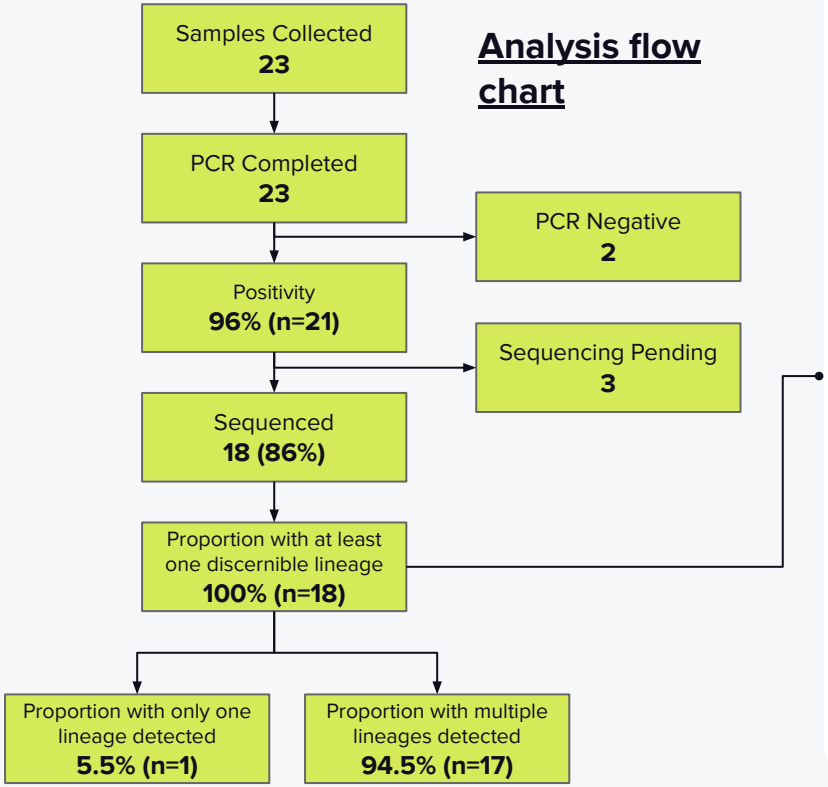






Aircraft → Lavatory Truck → Triturator → Terminal → Wastewater treatment plant

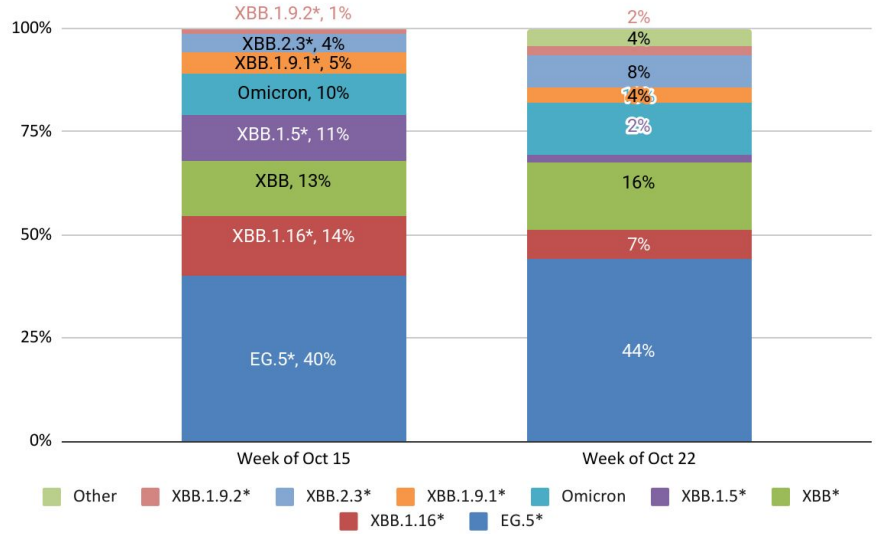
Whole Genome Sequencing shows a rich variety of SARS-CoV-2 lineages



Analysis flow chart

Deconvoluted lineage proportion

% of total lineage abundance, by collection date



Other category includes non-major lineages that have too low a resolution to call a sublineage

Collection period: Oct 16 - Oct 30

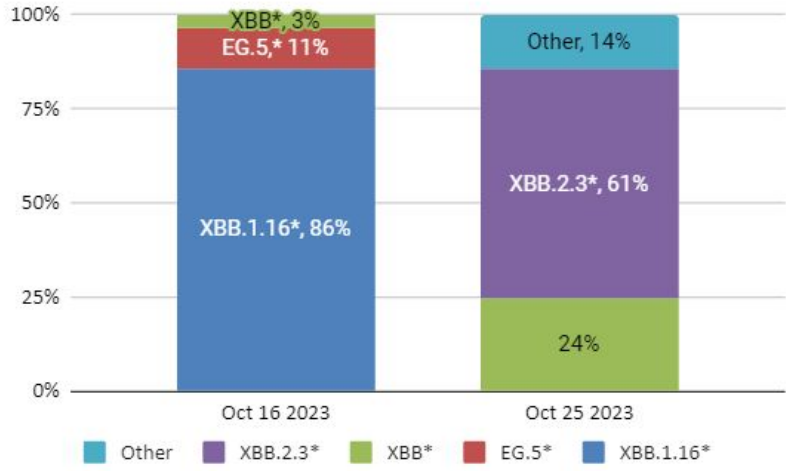
NOTE: Three samples were not included in sequencing because they arrived after the cut-off: 2 samples from BRU (10/25 and 10/30) and De-Identified Airport, France (10/30)

Results for 4 Aircraft Wastewater Samples from the US, UAE and China - with several samples containing multiple lineages

Deconvoluted lineage proportion

% of total lineage abundance, by collection date

Origin: US



Reference coverage *99%* *95%*

Origin: UAE

98%

Origin: China

90%

UAE: COVID case reporting stopped in May 2023; no SARS-CoV-2 sequences uploaded to global databases since Feb 2023

Result: SARS-CoV-2 (EG.5*) detected in an airport-collected aircraft wastewater sample from flight originating from UAE.

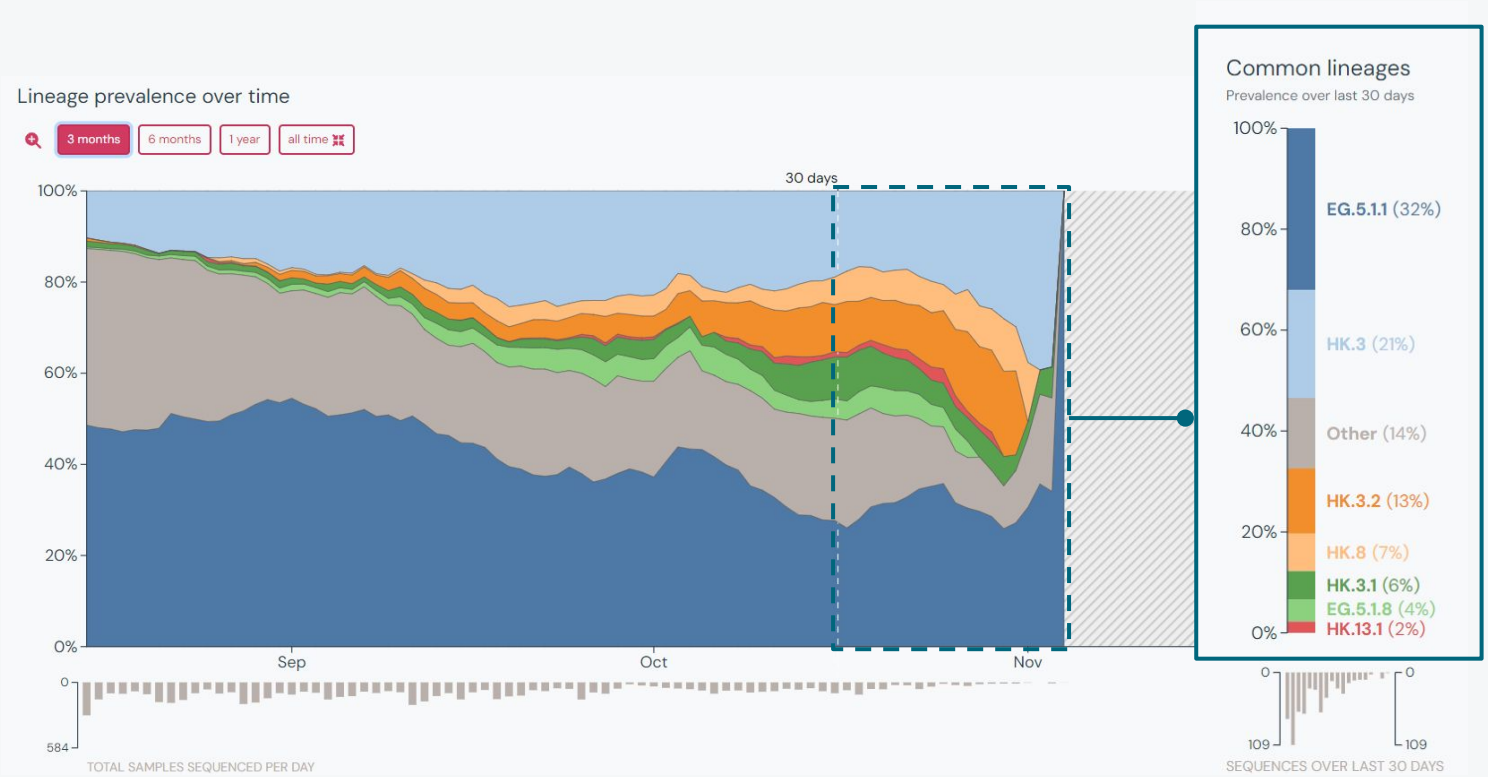
Discussion: Aircraft wastewater testing can shed light on global information blind spots

- **Low levels of SARS-CoV-2 epidemiologic and genomic surveillance** currently pose challenges for accurately understanding the disease burden and variant landscape.
- WHO reports that due to few sequences submitted from Africa, Eastern Mediterranean, and South-East Asia, **it has not been possible to determine trends for major variants in these regions**

Reported COVID-19 cases in UAE, 2023
Daily cases

Source: UAE National Emergency Crisis and Disaster Management Authority

China: Aircraft wastewater results are consistent with national picture, where EG.5 is the most common lineage



Source: Outbreak.info (data from GISAID), link

Learnings from the EU PoC and other programs that can be applied to a global scale-up

- Build upon established partnerships in the EU and globally - these initial partners are **the early adopters** and the program's **best promoters.**
- Set **lab and data standards** to ensure data comparability across the network. Set up data integration with partner laboratories.
- **Sample governance** (sample ownership, chain of custody).
- **Clear data sharing framework** is critical to ensure proper project launch.
- Drive towards **sustainability**, making the **program affordable** and easily **accessible**.
- Program can be a catalyst to **build local capacity** and maintain a warm infrastructure.
- **Public-private partnerships** are an effective tool to ensure rapid implementation and scalability, and encourage continuous technological innovation.

Thank you!

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Eszter Roka
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Airports
Brussels Airport
FRAport
Royal Schiphol Group
SEA Aeroporti di Milano
Others (not identified)

Country partners

Belgium (Sciensano)
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Koenraad Van Hoorde

France (Veolia)
Sebastien Lacroix
Jeremy Laplace
Romain Thiriat
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GINKGO BIOWORKS

Thank you

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