# INSaFLU-TELE-Vir: an open web-based bioinformatics suite for influenza and SARS-CoV-2 genome-based surveillance

Miguel Pinheiro<sup>‡</sup>, Ricardo J Pais<sup>§</sup>, Joana Isidro<sup>§</sup>, Miguel Pinto<sup>§</sup>, Carlijn Bogaardt<sup>I</sup>, Joaquin M Prada<sup>I</sup>, Daniel L Horton<sup>I</sup>, João P Gomes<sup>§</sup>, Vítor Borges<sup>§</sup>

‡ Institute of Biomedicine-iBiMED, Aveiro, Portugal

§ National Institute of Health Dr. Ricardo Jorge (INSA), Lisbon, Portugal

| University of Surrey, Surrey, United Kingdom

Corresponding author: Vítor Borges (vitor.borges@insa.min-saude.pt)

# Abstract

A new era of virus surveillance is emerging based on the real-time monitoring of virus evolution at whole-genome scale (World Health Organization 2021). Although national and international health authorities have strongly recommended this technological transition, especially for influenza and SARS-CoV-2 (World Health Organization 2021, Revez et al. 2017), the implementation of genomic surveillance can be particularly challenging due to the lack of bioinformatics infrastructures and/or expertise to process and interpret next-generation sequencing (NGS) data (Oakeson et al. 2017).

We developed and implemented INSaFLU-TELE-Vir platform (https://insaflu.insa.pt/) ( Borges et al. 2018), which is an influenza- and SARS-CoV-2-oriented bioinformatics free web-based suite that handles primary NGS data (reads) towards the automatic generation of the main "genetic requests" for effective and timely laboratory surveillance. By handling NGS data collected from any amplicon-based schema (making it applicable for other pathogens), INSaFLU-TELE-Vir enables any laboratory to perform multi-step and intensive bioinformatics analyses in a user-oriented manner without requiring advanced training.

INSaFLU-TELE-Vir handles NGS data collected from distinct sequencing technologies (Illumina, Ion Torrent and Oxford Nanopore Technologies), with the possibility of constructing comparative analyses using different technologies. It gives access to user-restricted sample databases and project management, being a transparent and flexible tool specifically designed to automatically update project outputs as more samples are uploaded. Data integration is thus cumulative and scalable, fitting the need for both routine surveillance and outbreak investigation activities.

The bioinformatics pipeline consists of six core steps:

- 1. read quality analysis and improvement,
- 2. human betacoronaviruses (including SARS-CoV-2 Pango lineages) and influenza type/subtype classification,
- 3. mutation detection and consensus generation,
- 4. coverage analysis,
- 5. alignment/phylogeny,
- 6. intra-host minor variant detection (and automatic detection of putative mixed infections).

The multiple outputs are provided in nomenclature-stable and standardized formats that can be visualized and explored *in situ* or through multiple compatible downstream applications for fine-tuned data analysis.

Novel features are being implemented into the INSaFLU-TELE-Vir bioinformatics toolkit as part of the OHEJP TELE-Vir (<u>https://onehealthejp.eu/jrp-tele-vir/</u>) project, including rapid detection of selected genotype-phenotype associations, and enhanced geotemporal data visualization.

All the code is available in github (<u>https://github.com/INSaFLU</u>) with the possibility of a local docker installation (<u>https://github.com/INSaFLU/docker</u>). A detailed documentation and tutorial is also available (<u>https://insaflu.readthedocs.io/en/latest/</u>).

In summary, INSaFLU supplies public health laboratories and researchers with an open and user-friendly framework, potentiating a strengthened and timely multi-country genome-based virus surveillance.

#### Keywords

Genomic surveillance; SARS-CoV-2; influenza; sequencing; bioinformatics; public health.

#### Presenting author

Vítor Borges

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### Hosting institution

National Institute of Health Dr. Ricardo Jorge (INSA), Lisbon, Portugal.

# **Conflicts of interest**

None.

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