Genetic diversity of the novel coronavirus SARS-CoV-2 (COVID-19) in Portugal

More information at **https://insaflu.insa.pt/covid19/**

Situation Report

7th June 2022

The **National Institute of Health Doutor Ricardo Jorge, I.P. (INSA)** has analysed **36424 SARS-CoV-2 genome sequences** so far, obtained from positive samples collected in more than 100 laboratories/hospitals/institutions, accross 304 municipalities.

The genetic diversity of SARS-CoV-2 has been monitored based on an average of 522 sequences/week, since the beginning of June, 2021. These sequences have been obtained from positive samples collected randomly throughout the **18 Districts of Portugal Mainland and the Autonomous Regions of the Azores and Madeira**, covering an average of 139 municipalities per week (**Figures 1 e 2**).

Figure 1. Geographic coverage (at the municipality level) of the last weekly nationwide sequencing survey, which resulted in 560 new SARS-CoV-2 genome sequences from 154 municipalities.

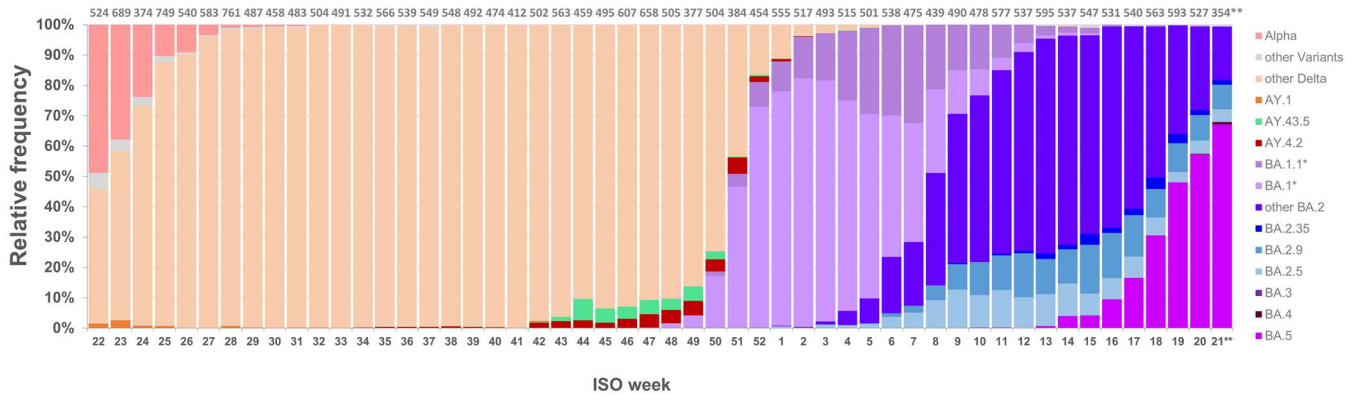

Figure 2. Evolution of the weekly relative frequency of the SARS-CoV-2 (sub-)lineages circulating in Portugal between ISO weeks 22 (31st May – 6th June, 2021) and 21 (23th – 29th May, 2022). The values on top of each bar indicate the number of sequences analysed per week in the context of the weekly random nationwide surveys. The plot highlights: i) BA.1 (and sub-lineage BA.1.1), BA.2 sub-lineages with relative frequency ≥1% in week 20 (sampling closed), BA.3, BA.4 and BA.5 lineages (all classified as *Omicron* by the WHO); ii) *Delta* sublineages of interest (AY.1, AY.4.2 e AY.43.5); and iii) the Alpha variant. *BA.1 = BA.1 and sub-lineages (with exception of BA.1.1 and sub-lineages). **The frequencies presented for the last week under analysis (ISO week 21) might change in the next report, given that some data from that period is still being processed. BA.1.1 = BA.1.1 and sub-lineages.

Bioinformatics Unit | Department of Infectious Diseases
NATIONAL INSTITUTE OF HEALTH DOUTOR RICARDO JORGE
Avenida Padre Cruz, 1649-016 Lisboa, PORTUGAL

Main highlights:

The Variant of Concern (VOC) *Omicron*, according to the WHO classification, currently includes several (sub)lineages identified by the "BA" prefix. The nomenclature of the various sub-lineages is under constant review and refinement (https://www.pango.network/). The sequences identified in Portugal are reclassified weekly and the result are available on our website https://insaflu.insa.pt/covid19/. Whenever relevant, some of these sub-lineages will be highlighted in this report.

- **Lineage BA.5**

  - Lineage BA.5 presents several genetic traits of interest, such as the presence of the mutations **L452R** and **F486V in Spike** (both affect Spike regions that interact with the human cells and mediate adherence/immune evasion). BA.5 also presents the deletion **del69-70 in Spike**, which is responsible for the **SGTF** profile, so this laboratory indicator can also be used as a proxy to estimate its frequency. The nationwide weekly surveys by sequencing, together with the daily monitoring of the proportion of samples with SGTF profile (**Figures 2** and **3**), show that, since its first detection in week 13, the **lineage BA.5 has been markedly increasing in relative frequency, being clearly dominant in Portugal since week 19 (9-15 May 2022) and presented a relative frequency of 68.9% in the last national sequencing survey in week 21** (**Figure 3**). Still, as data from this week are preliminary, a marked increase is espected. In fact, the SGTF data from the corresponding week already pointed towards a higher relative frequency (see previous report from 31 May).
    Note: Due to the recent decrease in the number of tests performed with the *TaqPath – ThermoFisher* methodology (allowing the monitoring of the proportion of samples with "SGTF" profile) by the different laboratories (see Figure 3 caption), SGTF data lack robustness and, as such, were not updated in the current report.

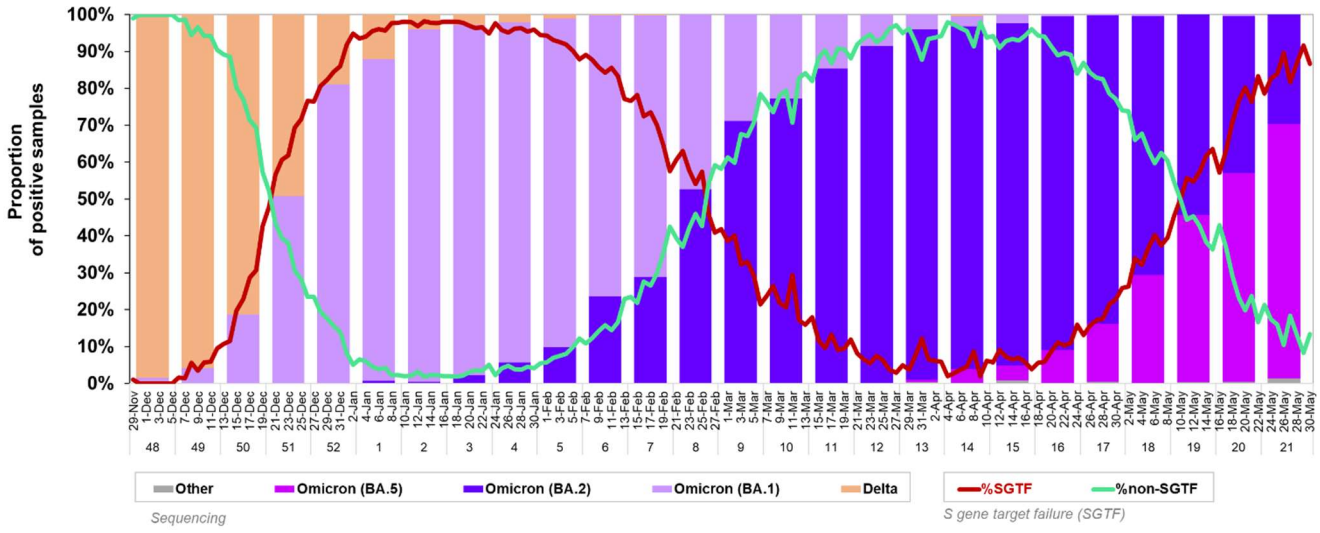

Figure 3. Evolution of the daily proportion of positive samples with and without S gene target failure (SGTF) in parallel with the relative frequency of the variants/lineages in circulation as assessed by the random nationwide sequencing surveys, since ISO week 48, 2021 (collection date). Currently, a **SGTF positive** sample is indicative of a probable case of **Omicron BA.5**, since lineage BA.1 has a residual circulation (<1% in week 16) in Portugal. A **non-SGTF positive** sample is indicative of a probable case of ***Omicron* BA.2**, since *Delta* (also "non-SGTF") has a residual circulation (<1%) in Portugal since week 5. The SGTF data analysis includes only positive samples tested with *TaqPath – ThermoFisher* with a *Cycle threshold* (Ct) ≤30 for the N and ORF1ab genes. The data relative to the most recents days (SGTF) or week (Sequencing) are provisional.

Source of SGTF data: laboratories using the kit TaqPath – ThermoFisher (UNILABS, a Cruz Vermelha Portuguesa, o Algarve Biomedical Center, SYNLAB, Hospital de Santo Espírito da Ilha Terceira e Universidade do Porto); See here the table with the data presented in the Figure.

- **Lineage BA.2**
  - **In Portugal, BA.2 has been firstly detected in random nationwide sequencing surveys in ISO week 52** (27th December 2021 – 2nd January 2022) (**Figure 2**), becoming **dominant on week 8 (21st–27th February 2022)**. After reaching a maximum relative frequency of 95% on week 13 (28th May – 3rd Abril 2022), this lineage presents a continuous descrease in relative frequency, having ceased to be dominant since week 19 (9th-15th May 2022), point from which lineage BA.5 became dominant in Portugal (**Figures 2, 3** and **4**).
  - **The sublineage BA.2.12.1 has revealed a relative frequency with increasing trend** between weeks 17 (0.4%) and 19 (1.3%), having presented a relative frequency of 0.8% in week 20**. This lineage has already been detected in all 7 Regions** (**Figure 4**), 12 districts in total. This lineage has raised particular interest internationally due to its **additional mutation** L452Q in Spike (affecting the same protein site described above) as well as due to its increasing circulation in some countries, namely in the United States of America.
  - **A sublineage of BA.2 (BA.2.35), with the additional mutation L452R in Spike protein, has been recently detected and is being monitored.** The L452R mutation is associated with resistance to neutralizing antibodies and is also known as a marker mutation of other variants of interest/concern, such as *Delta*, *Kappa* and *Omicron* BA.4/BA.5. **BA.2.35 relative frequency has shown an increasing trend** since its first detection on 1st March 2022 (ISO week 9), **reaching 3.6% of the sequences analysed in week 18**. Its frequency ranged from 1.7% to 2.9% in the subsequent nationwide sequencing surveys (*analysis ongoing*).

- **Lineage BA. 1**
  - **BA.1 has been firstly identified in Portugal by mid November, 2021, and was dominant between ISO weeks 51, 2021** (20th-26th November) **and 7, 2022** (14th-20th February), having reached its **maximum circulation in week 2 (95.6%, 10th- 16th January, 2022)** (**Figures 2** and **3**). The current circulation of BA.1 in Portugal is estimated to be residual (<1% since week 16, April 18th-24th, 2022).

- **Lineages BA.4 and BA.3**
  - **Since week 19 (May 9th-15th), 4 sequences of the BA.4 lineage of Omicron variant were identified in Portugal**, associated with confirmed cases in 4 out of the 7 Regions (**Figure 4**). Similarly to BA.5, with which it shares multiples mutations of interest, BA.4 lineage (also classified as VOC) has a relevant circulation in some countries, in particular in South Africa. In Portugal, no BA.3 case has been detected since week 11 (14-20 March 2022; see Report from 29 March 2022).

- **Recombinants**

  - The co-circulation of several lineages/variants in the community increases the possibility of the occurrence of mixed infections, i.e., the same individual is simultaneously infected by more than one of them. In this context, mixture of their genetic material might occur, resulting in a hybrid genetic profile, commonly designated as "recombinant".

  - Currently, several SARS-CoV-2 recombinants have been described at a global scale (e.g., Delta+Omicron BA.1 or BA.1+BA.2), with novel designations being assigned to the recombinants with epidemiological/functional relevance. **In Portugal, the few recombinant viruses identified so far were detected in sporadic cases** in the weekly random surveys. Among these, we highlight **cases associated with the recombinants internationally designated as XM, XN, XE and XH**, being that all are characterized by a hybrid genetic profile where an initial part of the genome corresponds to lineage BA.1 and the rest to lineage BA.2. In this report, it is also highlighted the detection of a potential recombinant between lineages BA.5 and BA.2.35, both co-circulating in Portugal for several weeks. Similarly to other recombinant SARS-CoV-2 detected so far in Portugal, there is no evidence that these recombinants might present functional differences (e.g., differences in transmissibility and immune evasion) from the parental lineages BA.1 and BA.2.

- Dynamic tables summarizing the **frequency and geotemporal spread of the variants/lineages identified so far as well as the mutations of interest in protein Spike** in each of them are available in the website.

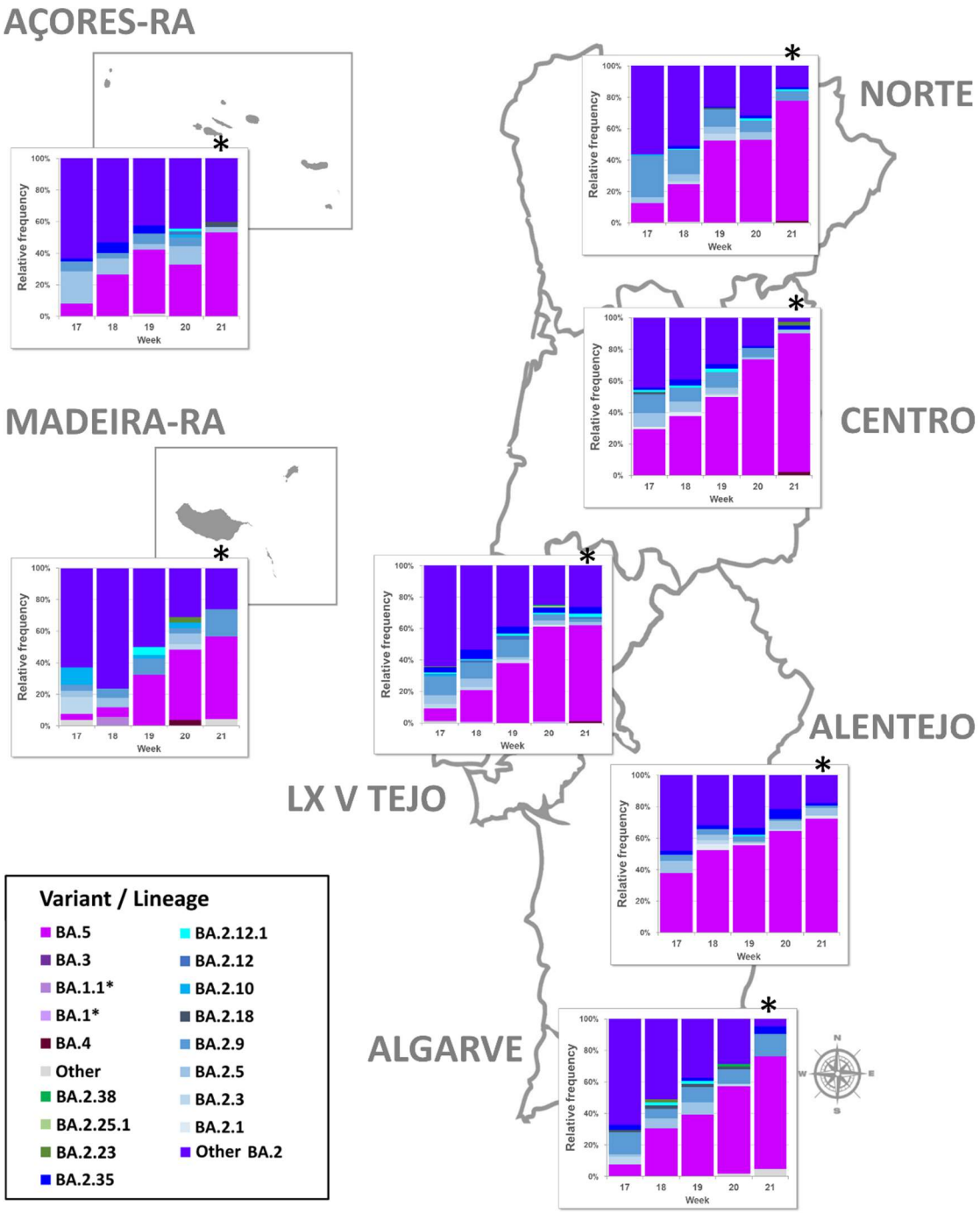

Figure 4. Evolution of the weekly relative frequency of SARS-CoV-2 lineages in each Health Region, between ISO weeks 17 (25 April-1 May) **and 21** (23–29 May), **2022**. The plots highlight the BA.1 (including its sublineage BA.1.1), BA.2 sub-lineages with relative frequency ≥1% in at least one Region in week 15 (sampling closed), BA.3, BA.4 and BA.5 (all classified as *Omicron* by WHO). BA.1.1 = BA.1.1 and sub-lineages; BA.1 = BA.1 and sub-lineages (with exception of BA.1.1 and descendent sub-lineages).

**It is expected that the frequencies presented for the last week under analysis (ISO week 21) might change in the next report, given that some data from that period is still being processed.*