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

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

Situation Report

26th April 2022

The **National Institute of Health Doutor Ricardo Jorge, I.P. (INSA)** has analysed **33101 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 138 municipalities per week (**Figures 1 e 2**).

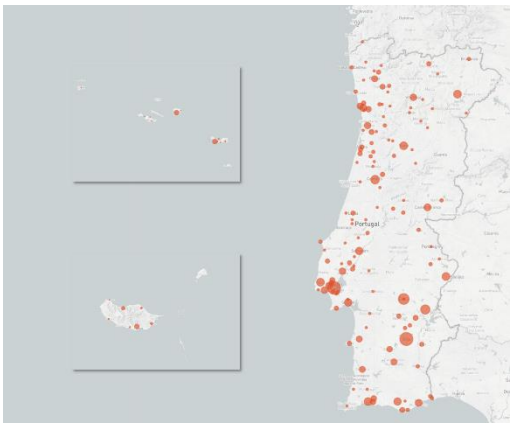

Figure 1. Geographic coverage (at the municipality level) of the last weekly nationwide sequencing survey, which resulted in 533 new SARS-CoV-2 genome sequences from 149 municipalities.

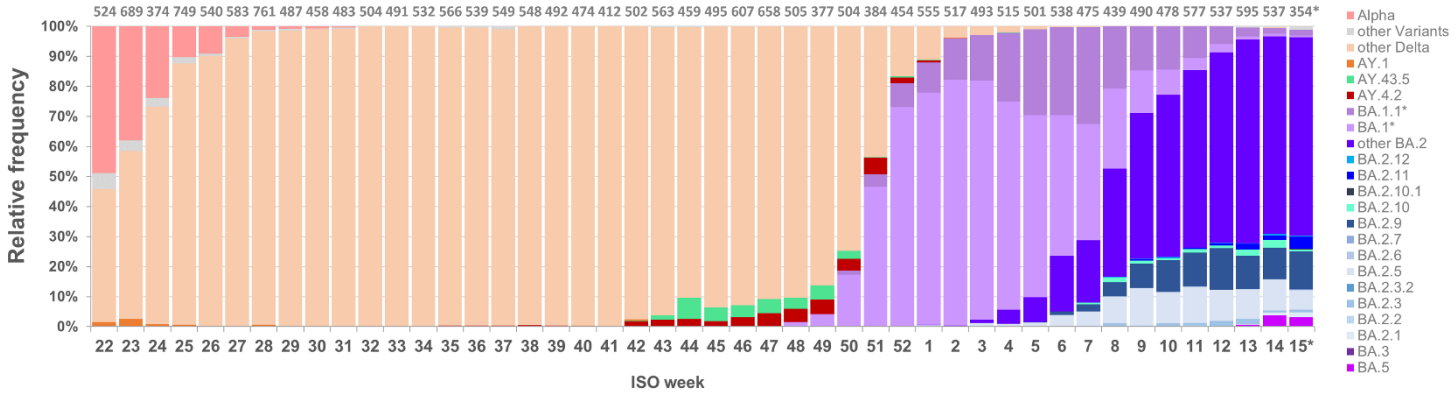

Figure 2. Evolution of the weekly relative frequency of the SARS-CoV-2 (sub-)lineages circulating in Portugal between ISO weeks 22 (31st May – 6th June, 2021) and 15 (11th – 17th April, 2022). The values on top of each bar indicate the number of sequences analysed per week in the context of the weekly random nationwide surveys. The plot highlights: i) BA.1 (and sub-lineage BA.1.1), BA.2 (and several sub-lineages), BA.3 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. *The frequencies presented for the last week under analysis (ISO week 14) 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; BA.1 = BA.1 and sub-lineages (with exception of BA.1.1 and sub-lineages).

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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.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). This lineage had an **estimated relative frequency of 2,5% on week 15 (11th-17th April 2022; *analysis ongoing*),** according to sequencing data (Figures 2 and 3). The evaluation of the proportion of SGTF (S gene target failure) positive samples, with the *TaqPath – ThermoFisher* kit, does not allow the estimation of the current relative frequency of lineage BA.1, since another lineage with this profile is also circulating (*see lineage BA.5 below*) (Figure 3).

- **Lineage BA.2**
  - When BA.1 was firstly identified in mid November 2021, another **lineage (BA.2) sharing several genetic traits,** including an excess of mutations in Spike (many of which shared), was also identified. Contrarily to BA.1, **BA.2 lineage does not harbor the del69-70 deletion in the Spike protein, and hence does not present S gene target failure (SGTF)**. **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)**. According to the proportion of non-SGTF positive samples (indicative of probable Omicron BA.2 case), **BA.2 is estimated to represent 86,9% of the positive samples on 25th April 2022** (Figures 2, 3 and 4).

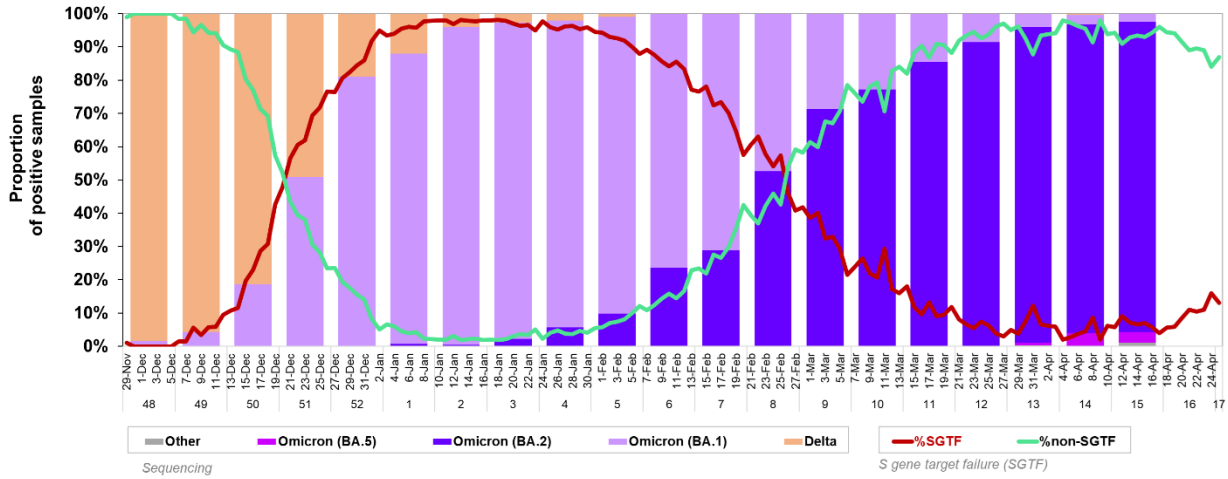

Figure 3. Evolution of the daily proportion of positive samples with and without S gene target failure (SGTF) in parallel with the relative frequency of the variants/lineages in circulation as assessed by the random nationwide sequencing surveys, since ISO week 48, 2021 (collection date). Currently, a **SGTF positive** sample is indicative of a probable case of **Omicron BA.1 (including its BA.1.1 sublineage)** or **Omicron BA.5** (also "SGTF"), since both are circulating (they represented ~3.6% and 2.0% of the sequences analysed on week 14, respectively) and lineage BA.3 (also "SGTF") is not detected since week 11. 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.

- Among the high genetic diversity currently observed among BA.2 sequences, we report the **detection of a genetic cluster characterized by the additional mutation L452R in Spike protein**. This 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* and *Kappa*. The first sequence bearing this genetic profile dates from 1st March 2022 (ISO week 9) and, since then, this sublineage (whose international designation is ongoing) has already been detected in **four Regions (North, Centre, Lisbon and Tagus Valley, and Alentejo)**, in a total of 17 municipalities. It represented 4.0% of the sequences analysed in week 15 (analysis ongoing).

- **Lineages BA.4 and BA.5**
  - Recently, two new *Omicron* lineages have been nominated, **BA.4** and **BA.5**. These lineages are descendants of lineage BA.2, presenting several genetic differences, 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). Although there are still few sequences globally available from these lineages, the majority also presents the deletion **del69-70 in Spike**, which is responsible for the **SGTF** profile, contrarily to the currently dominant lineage (BA.2, with non-SGTF profile) (**Figure 3**). In Portugal, after its detection in week 13, **lineage BA.5 has been increasing in relative frequency, already reaching >3% in the nationwide sequencing surveys of ISO weeks 14 and 15** (4th-17th April 2022; *ongoing analysis*), and circulating with higher intensity (>4% on week 15, analysis ongoing) in the North, Centre and Alentejo Regions (**Figure 4**). SGTF data from week 16 (**Figure 3**) suggests that BA.5 relative frequency is continuously increasing. So far, no BA.4 case has been detected in Portugal.

  - **We highlight that BA.5, together with the sublineage BA.2+S:L452R** (described above)**, are the two main lineages of interest that present an increasing relative frequency in Portugal.**

- **Lineage BA.3**

  - 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. 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.

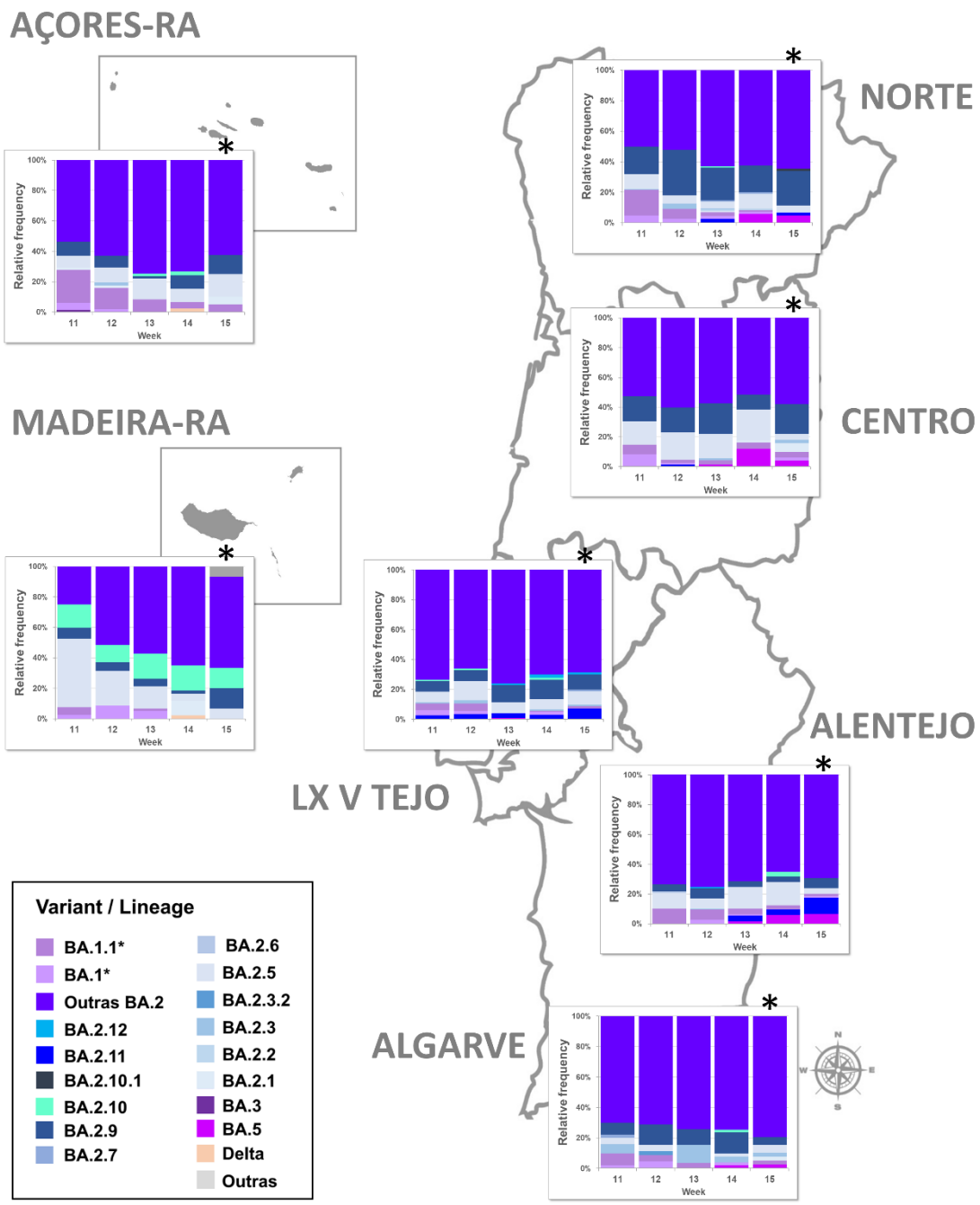

Figure 4. **Evolution of the weekly relative frequency of SARS-CoV-2 lineages in each Health Region, between ISO weeks 11** (14th – 20th March) **and 15** (11th – 17th April) **2022**. The plots highlight the BA.1 (including its sublineage BA.1.1), BA.2 (and several sub-lineages), BA.3 and BA.5 (all 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 14) might change in the next report, given that some data from that period is still being processed.*

- 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.