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

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

Situation Report

10th May 2022

The **National Institute of Health Doutor Ricardo Jorge, I.P. (INSA)** has analysed **34193 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 523 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**).

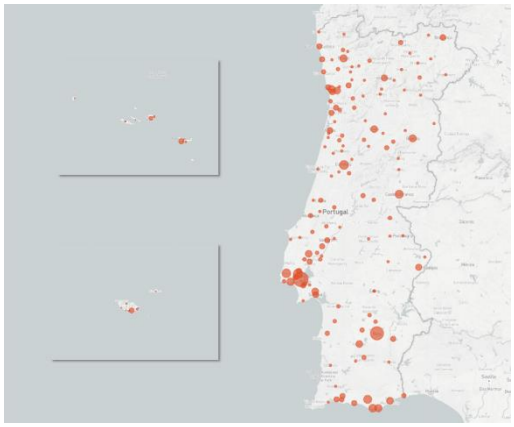

Figure 1. Geographic coverage (at the municipality level) of the last weekly nationwide sequencing survey, which resulted in 544 new SARS-CoV-2 genome sequences from 153 municipalities.

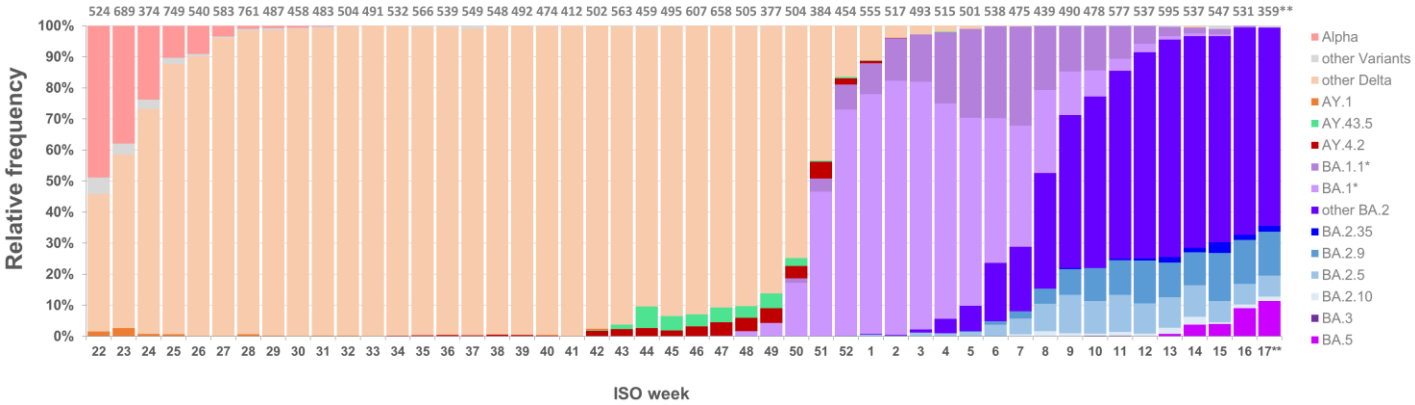

Figure 2. Evolution of the weekly relative frequency of the SARS-CoV-2 (sub-)lineages circulating in Portugal between ISO weeks 22 (31st May – 6th June, 2021) and 17 (25th April – 1st May, 2022). The values on top of each bar indicate the number of sequences analysed per week in the context of the weekly 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 15 (sampling closed), 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. *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 17) 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.

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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.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)**. According to the proportion of non-SGTF positive samples (indicative of probable Omicron BA.2 case), **BA.2 relative frequency shows a decreasing trend and is estimated to be 62.9% on 8 May 2022** (**Figures 2, 3** and **4**).

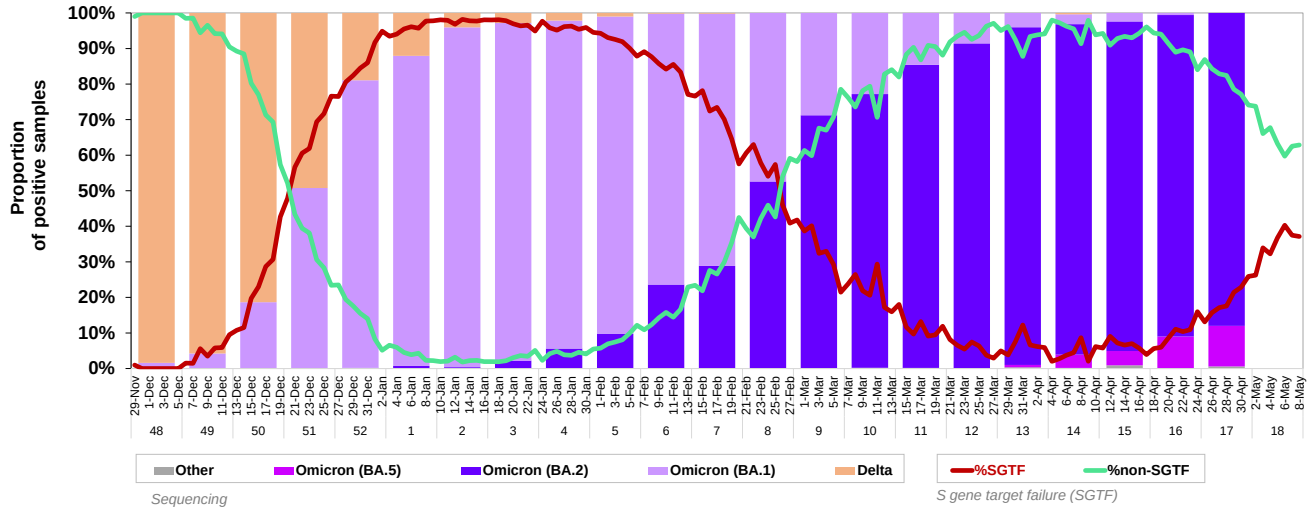

Figure 3. Evolution of the daily proportion of positive samples with and without S gene target failure (SGTF) in parallel with the relative frequency of the variants/lineages in circulation as assessed by the random nationwide sequencing surveys, since ISO week 48, 2021 (collection date). Currently, a **SGTF positive** sample is indicative of a probable case of **Omicron BA.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.

  - **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* and *Kappa*. Since its first detection on 1st March 2022 (ISO week 9), this sublineage presented a frequency with an increasing trend until week 15, when it represented 3.5% of the sequences analysed. During the following weeks, this trend has reversed, with BA.2.35 registering frequencies <2% until week 17 (sampling ongoing).

  - Sequences of the **sublineage BA.2.12.1** have been identified for the first time in Portugal, associated with two cases in the Centre and Lisbon and Tagus Valley Regions (**Figure 5**) . 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.

- **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). Contrarily to the currently dominant lineage BA.2, BA.5 presents the deletion **del69-70 in Spike**, which is responsible for the **SGTF** profile (Figure 3). In Portugal, after its detection in week 13, **lineage BA.5 has been increasing in relative frequency, having duplicated its relative frequency between ISO weeks 15 (4.0%, 11-17 April) and 16 (9.0%, 18-24 April)** (analysis and sampling concluded) (Figure 2). The nationwide sequencing survey of week 17 (ongoing), together with the proportion of samples with SGTF profile, indicate that this **trend of duplication of the relative frequency by week has continued, and it is estimated that BA.5 represented ~37% of the positive cases by 8 May 2022** (Figure 3).

  - **It is forecasted that BA.5 lineage can reach a relative frequency of ~80% on May 22nd, 2022** (Figure 4), assuming a **growth rate (relative) of 13%** (95%CI: 12% to 14%) **per day and a doubling time of about 6 days** (Figure 4). This forecasting does not include the possibility of the emergence of other lineages with SGTF profile and/or other lineages with increased competitive advantage.

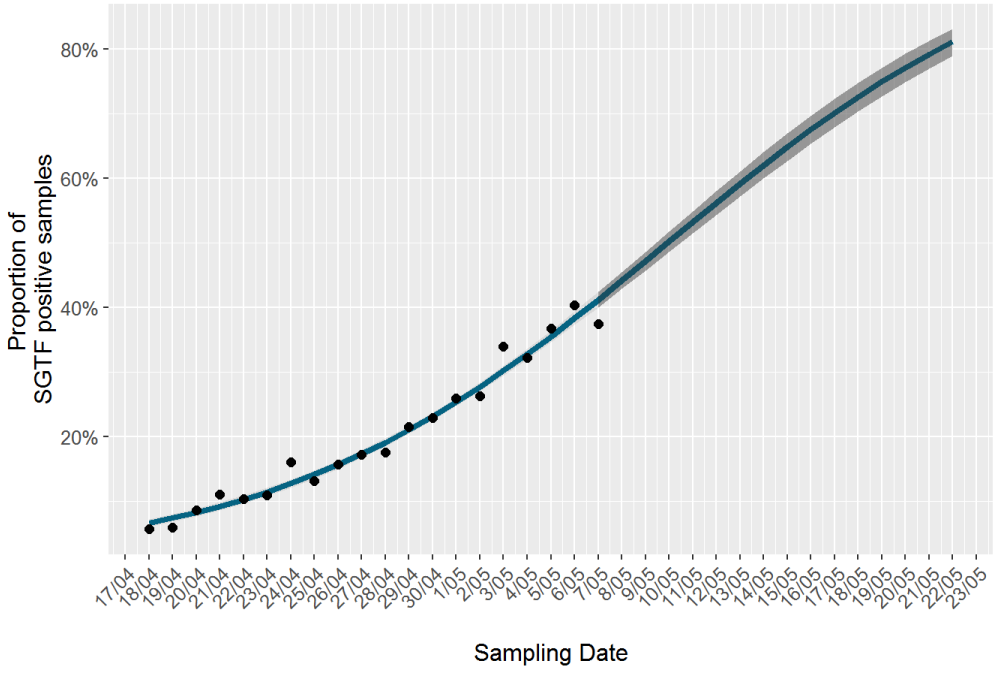

Figure 4. **Evolution of the proportion of positive samples with S gene target failure (SGTF) in Portugal** during the period from April 18th to May 7th (black dots), 2022, together with a **15-day forecast of the growth trend** using a binomial logistic model, with a 95% confidence interval. The SGTF data analysis includes only positive samples tested with *TaqPath – ThermoFisher* with a *Cycle threshold* (Ct) ≤30 for the N and ORF1ab genes. Currently, a **SGTF positive** sample is indicative of a probable case of **Omicron BA.5**, since lineage BA.1 has a residual circulation in Portugal (<1% in week 16 – starting point used to forecast the relative frequency of BA.5 based on SGTF data).

- **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, and, so far, no cases have been detected on week 17 (analysis ongoing).

- **Lineages BA.3 and BA.4**
  - In Portugal, no BA.3 case has been detected since week 11 (14-20 March 2022; see Report from 29 March 2022). So far, no BA.4 case has been detected in Portugal.

- **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.

- 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.

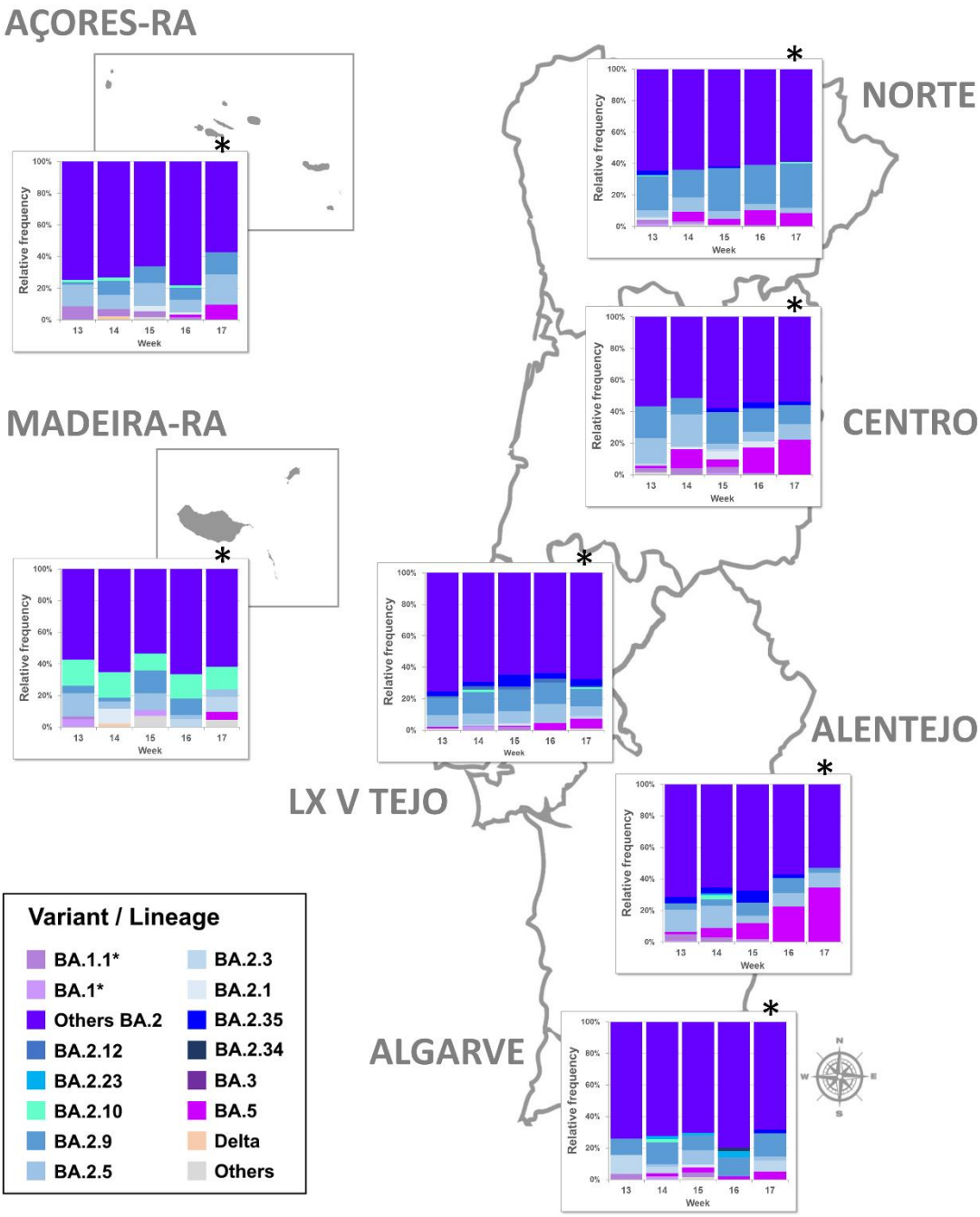

Figure 5. Evolution of the weekly relative frequency of SARS-CoV-2 lineages in each Health Region, between ISO weeks 13 (28 March – 3 April) **and 17** (25 April – 1 May), **2022**. The plots highlight the BA.1 (including its sublineage BA.1.1), BA.2 sub-lineages with relative frequency ≥1% in at least one Region in week 15 (sampling closed), BA.3 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 17) might change in the next report, given that some data from that period is still being processed.*