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

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

Situation Report

12th April 2022

The **National Institute of Health Doutor Ricardo Jorge, I.P. (INSA)** has analysed **31984 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 520 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 137 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 548 new SARS-CoV-2 genome sequences from 144 municipalities.

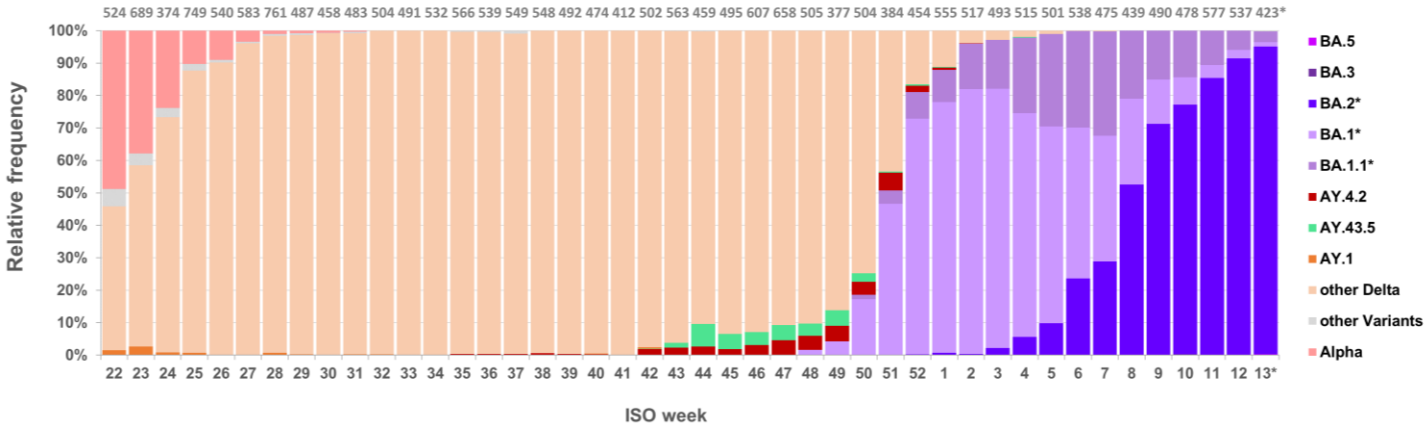

Figura 2. Evolution of the weekly relative frequency of the SARS-CoV-2 (sub-)lineages circulating in Portugal between ISO weeks 22 (31st May – 6th June, 2021) and 13 (28th March – 3rd April, 2022). The values on top of each bar indicate the number of sequences analysed per week in the context of the weekly random nationwide surveys. The plot highlights: i) the BA.1, BA.1.1, BA.2, BA.3 and BA.5 (sub)lineages (classified as *Omicron* by the WHO) and ii) *Delta* sublineages of interest (AY.1, AY.4.2 e AY.43.5). *The frequencies presented for the last week under analysis (ISO week 13) 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.2 = BA.2 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 5,8% on 11th April 2022,** according to the proportion of SGTF (S gene target failure) positive samples, with the *TaqPath – ThermoFisher* kit (**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**), when it started an increasing trajectory 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 94,2% of the positive samples on 11th April 2022** (**Figures 2, 3** and **4**).

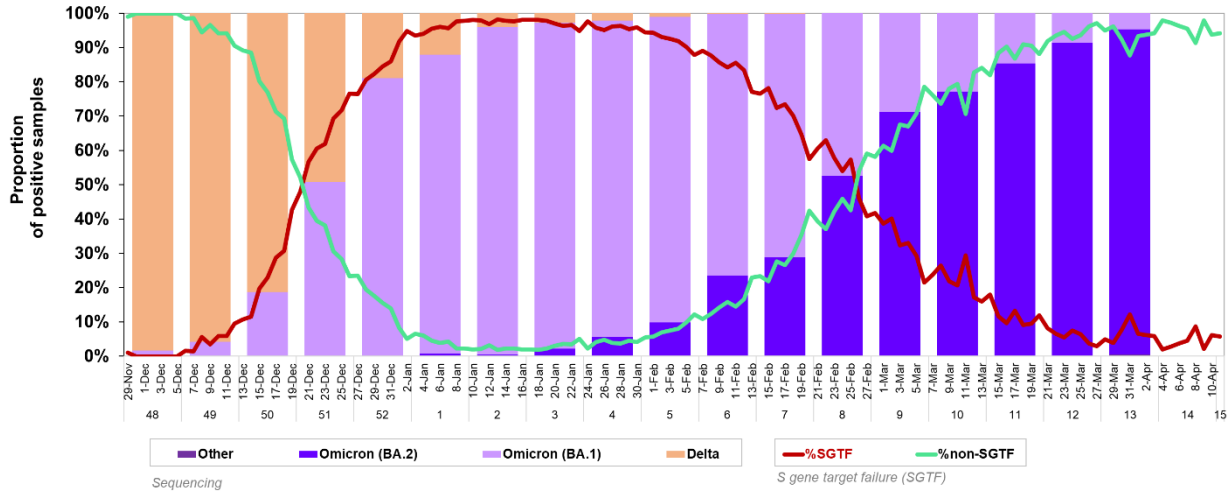

Figure 3. Evolution of the daily proportion of positive samples with and without S gene target failure (SGTF) in parallel with the relative frequency of the variants/lineages in circulation as assessed by the random nationwide sequencing surveys, since ISO week 48, 2021 (collection date). Currently, a **SGTF positive** sample is indicative of a probable case of ***Omicron* BA.1 (including its BA.1.1 sublineage)**, since BA.3 and BA.5 (also "SGTF") have only been detected at a relative frequency <0.5%. A **non-SGTF positive** sample is indicative of a probable case of ***Omicron* BA.2**, since *Delta* (also "non-SGTF") has not been detected in Portugal for several weeks. 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). Since then, it has been detected in four Regions (North, Centre, Lisbon and Tagus Valley, and Alentejo), in a total of 11 municipalities.

- **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, **lineage BA.5** was detected in a single case in the nationwide sequencing survey of ISO week 13 (28th March - 3rd April 2022; *ongoing analysis*), in the **Region of Lisbon and Tagus Valley** (**Figure 4**). So far, no BA.4 case has been detected in Portugal.

- **Lineage BA.3**
  - This *Omicron* lineage has been sporadically detected worldwide. In Portugal, BA.3 has only been detected in two cases in the random surveys of ISO weeks 10 and 11 (7th – 20th March, 2022) in the **Autonomous Region of the Azores** (**Figure 4**), with the phylogenetic analysis suggesting that they might be epidemiologically related. No BA.3 case was detected in weeks 12 and 13 (*ongoing analysis*).

- **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 **a case associated with the recombinant internationally designated as "XM"**, detected in week 13 (28th March – 3rd April, 2022; *ongoing analysis*) in the Centre Region, that is characterized by a hybrid genetic profile, where the first half of the genome corresponds to BA.1 and the second half to BA.2. The recombinant "XM" has been mostly identified in Germany and in the Netherlands, with no evidence that it might present functional differences (e.g., differences in transmissibility and immune evasion) from its parental lineages BA.1 and BA.2.

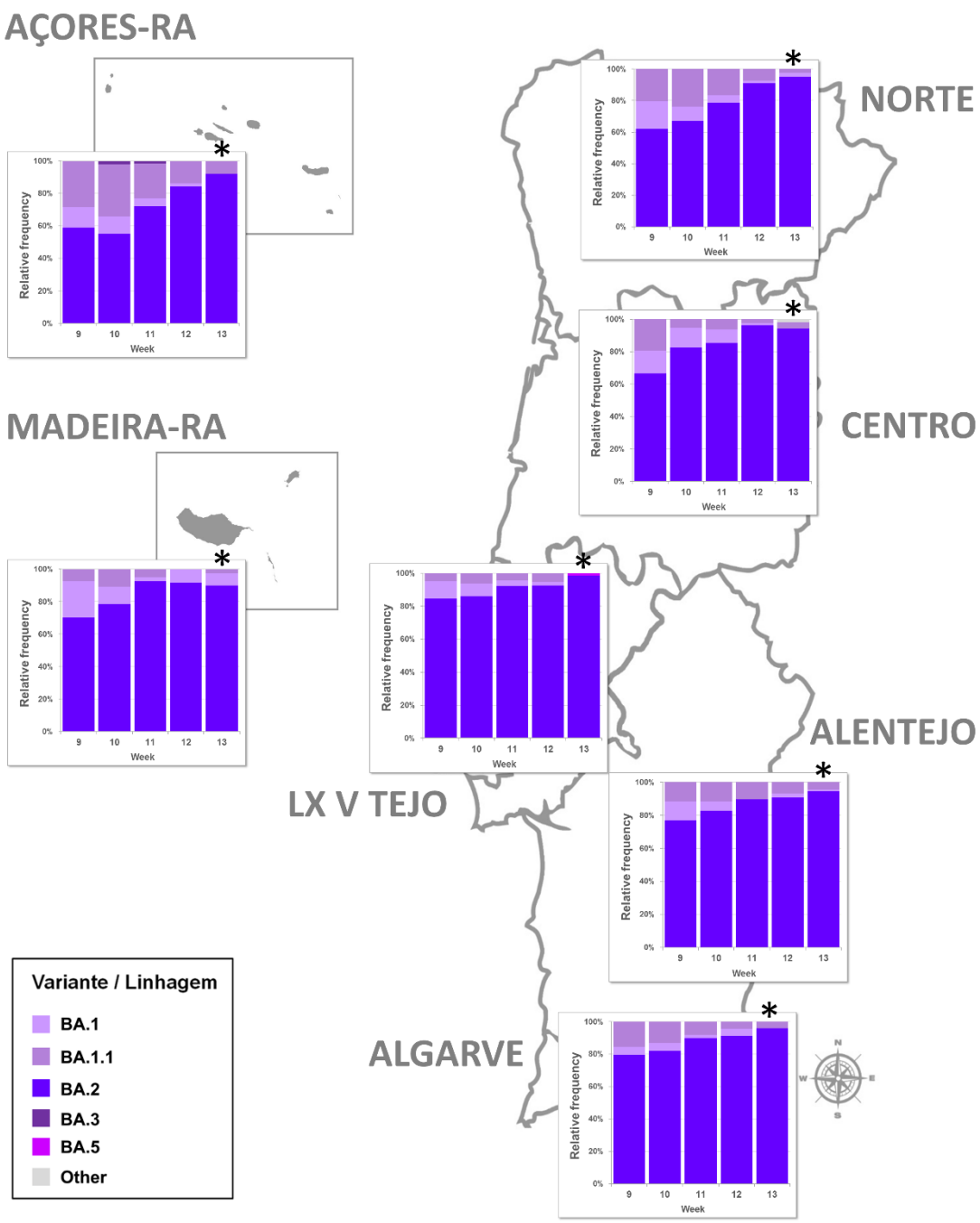

Figure 4. Evolution of the weekly relative frequency of SARS-CoV-2 lineages in each Health Region, between ISO weeks 9 (28th February – 6th March) **and 13** (28th March – 3rd April) **2022**. The plots highlight the BA.1 (including its sublineage BA.1.1), BA.2, BA.3, B.4 and BA.5 (classified as *Omicron* by WHO). BA.1.1 = BA.1.1 and sub-lineages; BA.2 = BA.2 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 13) 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.

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