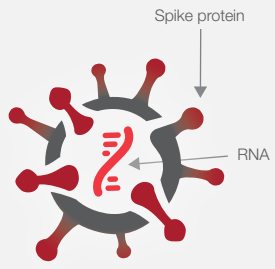
COVID-19 testing and the S gene target failure: get the facts

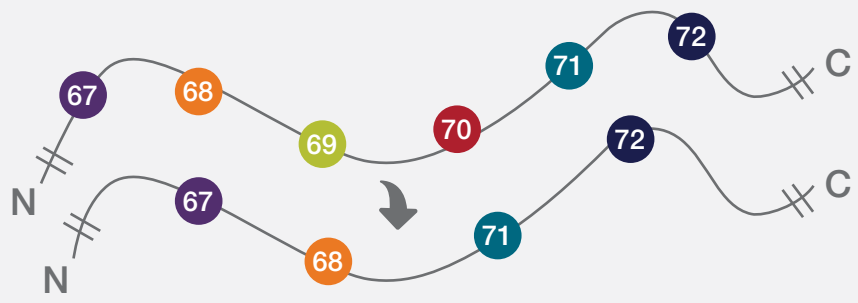
1 The S gene/protein



- SARS-CoV-2 has an RNA genome that encodes many proteins
- The **spike protein**, which is encoded by the **S gene**, is crucial for SARS-CoV-2 to attach to and infect target cells
- The spike protein is also a main target for many vaccines, medications, and diagnostics for COVID-19

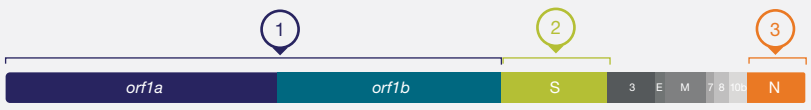
2 The 69-70del mutation

- Viruses constantly **mutate** leading to the emergence of new **variants**; mutations can occur anywhere in the viral genome
- The 69-70del mutation in the S gene is a **six-nucleotide deletion** (21,765–21,770), **removing two amino acids** at sites 69 (histidine) and 70 (valine) in the spike protein
- The 69-70del mutation was initially predominantly observed in the Alpha variant of SARS-CoV-2
- The **Omicron variant** has over 30 mutations in the S gene, including the 69-70del mutation
- Note: The Omicron variant is diverse, and includes the BA.1, BA.2, and BA.3 sub-lineages; the BA.2 sub-lineage does not have the 69-70del mutation (giving it the nickname "stealth Omicron"[1])



3 TaqPath COVID-19 diagnostic assay design

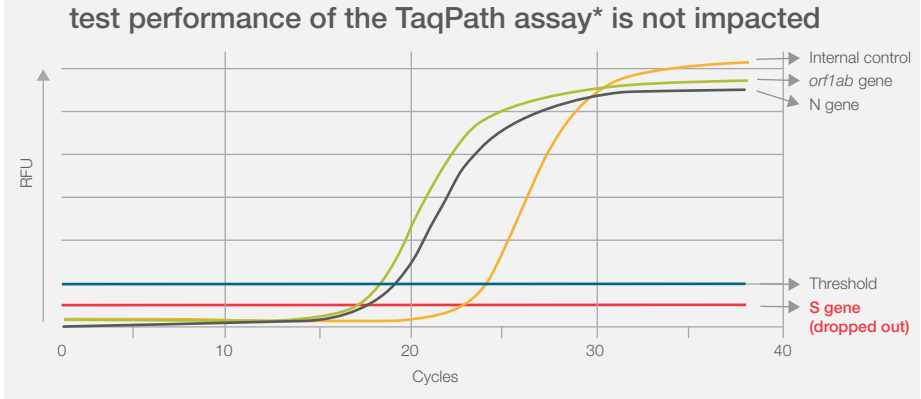
- The Applied Biosystems™ TaqPath™ COVID-19 diagnostic tests were designed as multi-target assays with **built-in redundancy** to compensate for mutations
- The first-generation assays* detect SARS-CoV-2 infections by **identifying the presence of three gene targets from the *orf1ab*, S, and N regions** of the virus
  - A positive result is called if at least two of the three SARS-CoV-2 targets are detected
  - A negative result is only called if none of the three SARS-CoV-2 targets is detected



3-target design

4 The S gene target failure

- The 69-70del mutation interferes with the detection of the S gene target by the TaqPath COVID-19 assay*, rendering the S gene target as not detected
- This is known as **S gene target failure (SGTF)** or S gene dropout
- The 69-70del mutation is the only currently known mutation that impacts detection of one of the three targeted sequences by the TaqPath assay*
- Most importantly, due to the multi-target test design, **the overall test performance of the TaqPath assay* is not impacted**



5 The S gene advantage

- With the TaqPath COVID-19 assay*, samples containing the Alpha and Omicron variants show SGTF in the majority of cases
- This is the **S gene advantage**—a surveillance tool that can be used to help aid in the identification of Alpha and Omicron
- Due to the novelty and potential risks associated with the Omicron variant, **further characterizing specimens that show SGTF using sequencing is recommended** (Sanger or next-generation sequencing)

The World Health Organization (**WHO**)[2], the US Food and Drug Administration (**FDA**)[3], the US Centers for Disease Control and Prevention (**CDC**)[4], and the European Centre for Disease Prevention and Control (**ECDC**)[5] **have all reported that using SGTF of PCR assays as a proxy helps in identifying the Omicron variant**

Notes

* In reference to the original TaqPath COVID-19 diagnostic assays:

- Applied Biosystems™ TaqPath™ COVID-19 Combo Kit: For Emergency Use Authorization (EUA) only. For prescription use only. For *in vitro* diagnostic use.
- Applied Biosystems™ TaqPath™ COVID-19 CE-IVD RT-PCR Kit: For *in vitro* diagnostic use.

References

1. https://www.ama-assn.org/delivering-care/public-health/what-ba2-or-stealth-omicron-subvariant
2. https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern
3. https://www.fda.gov/medical-devices/coronavirus-covid-19-and-medical-devices/sars-cov-2-viral-mutations-impact-covid-19-tests?utm_medium=email&utm_source=govdelivery#omicron-sgene
4. https://emergency.cdc.gov/han/2021/han00459.asp
5. https://www.ecdc.europa.eu/sites/default/files/documents/Implications-emergence-spread-SARS-CoV-2%20B.1.1.529-variant-concern-Omicron-for-the-EU-EEA-Nov2021.pdf

Find out more at **thermofisher.com/covid19mutations**

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