

SARS-CoV-2 Variants of Concern

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Key points

- Numerous genetic mutations in Covid-19 virus initiating a pandemic.
- Description of all concerned variants, their genetic and morphological modifications leading to major outbreaks.

Introduction

Since the beginning of 21st century, three variants of coronavirus have caused deadly pneumonia in humans: severe acute respiratory syndrome (SARS) in 2002, Middle-East respiratory syndrome coronavirus (MERS-CoV) in 2012 and SARS-CoV-2 in 2019.¹

Structure of Coronavirus

The principal structure of coronavirus has **four components**: viral envelope, spike proteins, membrane proteins and nucleocapsid. The spike protein consists of **three parts**: 1) **Receptor binding domain (RBD)** that recognizes Angiotensinogen Converting Enzyme Receptor 2 (ACE2) present in lungs, heart, kidney and intestine of host. **Two functional sub units** 2) **S1** that binds to host cell receptor and 3) **S2** that mediates the fusion of viral and cellular membranes. Mutation in the gene coding for spike protein causes formation of different strains. D614G is the mutated form of SARS-CoV-2 that triggered the pandemic in Feb'2019.²

Variants of Concern

A variant of concern (VOC) is the variant which is suspected to have increased transmissibility and reduced vaccine induced protection. **By far, four variants of concern of SARS-CoV-2** have been identified:

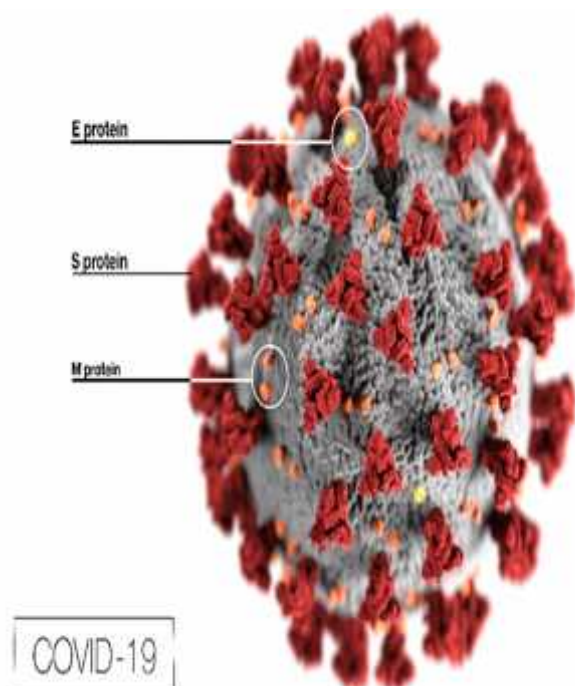


Figure 1 Structure of Covid-19 virus
(Source: phil.cdc.gov)

WHO label	Pango lineages	GISAID clade	Nextstrain clade	Additional amino acid changes monitored	earliest documented samples	Date of designation
Alpha	B.1.1.7	GRY	20I (V1)	+S:484K +S:452R	United Kingdom, Sep-2020	18-Dec-2020
Beta	B.1.351 B.1.351.2 B.1.351.3	GH/501Y/V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1 P.1.1 P.1.2	GR/501Y/V3	20J (V3)	+S:681H	Brazil, Nov-2020	11-Jan-2021
Delta	B.1.617.2 AY.1 AY.2	GR/478K/V1	21A	+S:417N	India, Oct-2020	VOC: 4-Apr-2021 VOC: 11-May-2021

Figure 2 Variants of Concern
(Source: who.int)

Alpha variant further has three mutations: 1) **N501Y** in which substitution of asparagine (N) by tyrosine (Y) at 501 position occurs, inflating ACE2 receptor binding affinity. 2) **HV69/70** mutation in which there is deletion of 69th and 70th amino acid in spike protein, causing change in particular part of S protein and evading neutralization of antibodies³ and 3) **P618H** in which there is substitution of proline (P) by histidine (H) at 618 position, elevating the activity of trans membrane protease (TMPRSS2) at furin cleavage sites leading to enhanced receptor mediated endocytosis.⁴

Beta and Gamma variant have two mutations: 1) **N501Y** (elaborated above) and 2) **E484K** in which glutamic acid (E) is substituted by lysine (K) at 484 position affecting receptor binding motif of RBD, increasing affinity to receptor.

Delta variant has two mutations: 1) **P681R** in which proline (P) is replaced by arginine (R) at 681 position that enhances and accelerates viral fusion and 2) **L452R** in which leucine (L) is replaced by arginine (R) at 452 position, escalating ACE2 receptor binding ability and reducing effect of vaccine stimulated antibodies.

Conclusion

Covid-19 has shown multiple strains during a short period of time. The virus is highly diverse and astonishingly adaptable inciting enormous fatalities across the globe. Extensive research work, the development of vaccines and other preventive measures have played a great role in bringing down the positivity rate of COVID-19. However, with development of modified strains, continuous endeavours are required to control the spread of the virus and to cure the ones already infected.

References

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