

Article

Emergence of Lambda Variant with Reduced Antibody Response; are We Facing another Worst Wave?

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The variant, variant of concern (VOC), and the variant of interest (VOI) of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pose a threat due to higher transmission rates, increased virulence, and weakened vaccine protections, as well as reduced neutralizing antibody-based therapeutics, posing a new challenge, particularly in low- and middle-income countries where vaccination is not widely available. Multiple variants of SARs-CoV-2; Variants B.1.351 (Beta), B.1.617.2 (Delta), B.1.427/B.1.429 (Epsilon), B.1.526 (Iota), and B.1.1.248 (Gamma) epress L452R, E484K, E484Q mutation in spike protein binding receptor enables neutralization of antibody of vaccinated individuals as well as reduced efficacy [1], [2], [3], [4], [5].

The recent emergence of lambda variant (C.37) in Peru and South America raises the risk of another wave of SARS-CoV-2 spreading around the world. While hundreds of lineages circulated at the same time, the SARS-CoV-2 C.37 spread quickly throughout South America, implying a higher transmissibility of that lineage [5], [6]. On June 14, 2021, the World Health Organization designated lambda variant as a variant of interest (<https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/>). The whole-genome sequencing and GSAID entry revealed that the lambda variant C.37 contains a unique deletion in the spike protein of SARS-CoV-2 at 247-253 positions in the N-terminal domain (NTD), as well as six nonsynonymous novel mutations named T76I, L452Q, G75V, F490S, D614G, and T859N in the spike gene of SARS-CoV-2 that are highly (more than 90%) conserved. SARS-CoV-2 C.37 also has an unique deletion in the ORF1a gene at locations 3675-3677, which is similarly seen in Alpha, Beta, and Gamma variants of the virus [7], [8].

The L452Q substitution mutation is unique to this form, and the F490S and L452Q mutations occur in the spike protein's RBD (receptor-binding domain). The delta variation (B.1.617.2) has the VOC mutation, the Epsilon variant (B.1.429/B.1.427/) has the VOI mutation, and the kappa variant (B.1.617.1) has the VOI mutation, which is responsible for their greater infectivity. The L452Q and T76I substitution mutations cause increased binding affinity of the spike protein for the ACE2 (abbreviation) receptor, which increases lineages transmissibility, whereas the L452Q and F490S mutations cause susceptibility to re-infection as well as decreased neutralizing antibody efficiency in vaccinated and unvaccinated individuals. The lambda variant (C.37) of SARS-CoV-2 is capable of evading vaccine-induced neutralizing antibodies due to the presence of a large, unique, and extremely conserved 7-amino-acid deletion in the NTD of the lambda spike protein called RSYLTPGD246-253N [5], [7], [8] (<https://www.tbsnews.net/tags/lambda-variant>).



Academic Editor: Dr. Md. Abu Saleh

Received: 12 April 2026

Revised: 1 May 2026

Accepted: 4 May 2026

Published: 16 May 2026

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In summary, the L452Q and T76I substitution mutation of the lambda variant (C.37) improve viral transmissibility, whereas the three alterations RSYLTPGD246-253N, F490S, and L452Q exhibit resistance to antiviral immunity in a vaccine-induced individual [7], [8].

Funding: Authors received no funding from an external source.

Declaration of Interest: The authors declare no conflict of interest.

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