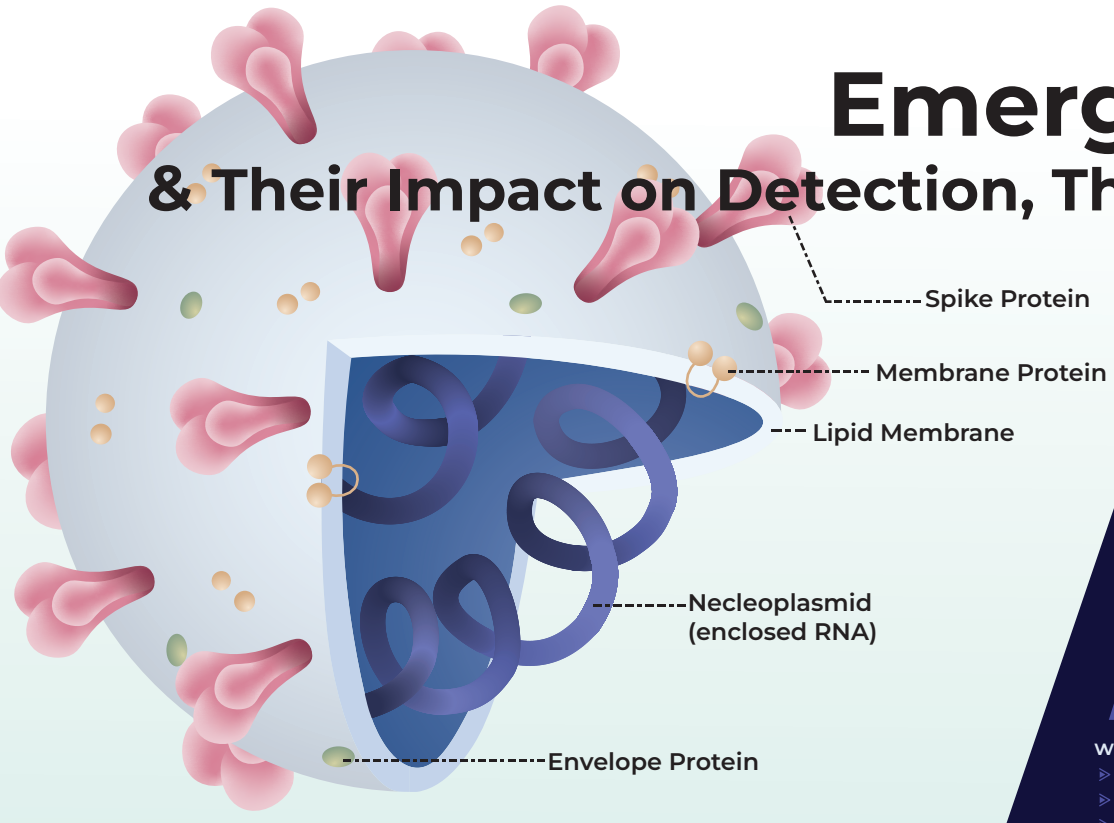
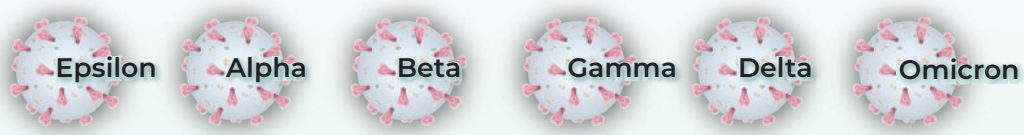
Emerging COVID-19 Variants

& Their Impact on Detection, Therapeutic Strategies & Vaccination



SARS-CoV-2 STRUCTURE

Emerging COVID-19 Variant of Concern till March 2022



What is Variant of Concern (VOC)?

Definition by World Health Organization (WHO)

SARS-CoV-2 VOC refers to a SARS-CoV-2

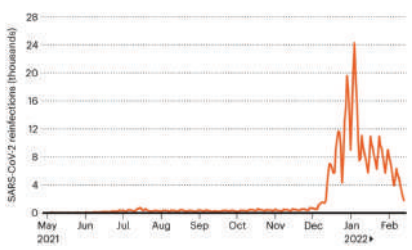
that meets the criteria of Variant of Interest (VOI)
- with genetic changes that are predicted or known to affect virus characteristics
- identified to cause significant community transmission or multiple COVID-19 clusters

with additional possible attributes of a VOI
- Increase in Transmissibility or detrimental change in COVID-19 epidemiology
- Increase in Virulence or change in clinical disease presentation
- Decrease in Effectiveness of public health and social measures or available diagnostics, vaccines, therapeutics

From the recorded data in UK, look into how Omicron overtook Delta

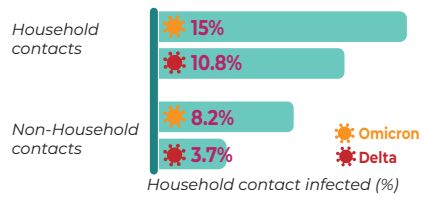
1 Rising Re-Infection

More than 650, 000 people in England have probably been infected with the coronavirus **twice**. Most of those reinfections have occurred since the Omicron variant was first detected last November.



Source:
Nature. *(2022).* COVID reinfections surge during Omicron onslaught. Retrieved on 10th March 2022, from https://www.nature.com/articles/d41586-022-00438-3.

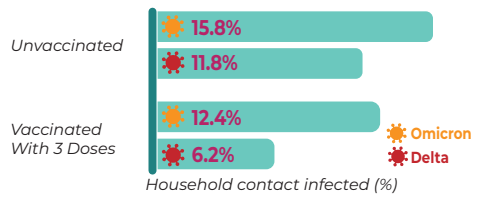
2 Rising Transmission



*** Household contact** refers to the contact if you are living with someone who has tested positive for COVID-19.

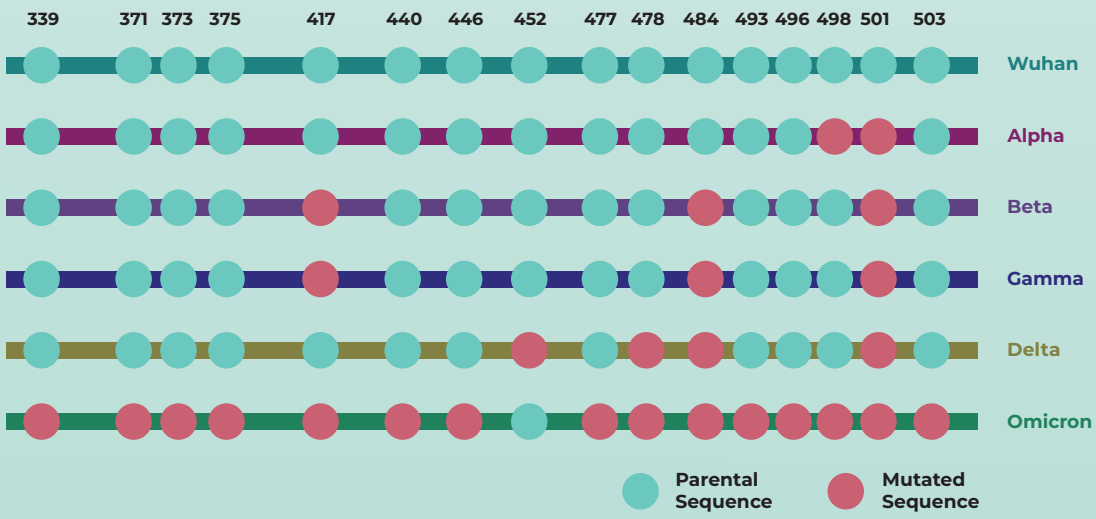
People infected with the Omicron variant pass it on to more close contacts than people infected with the Delta variant, regardless of their vaccination status.

3 The Vaccination Effect in Transmission



Overall, people who has received 3 vaccination doses are less likely to spread the Delta or Omicron variants to household members than an unvacinnated person. But vaccines are not as efficient at blocking transmission.

Source:
[1] Nature. *(2022).* COVID-19: How Omicron overtook Delta in three charts. Retrieved on 10th March 2022, from https://www.nature.com/articles/d41586-022-00632-3.
[2] Allen, H., Tessier, E., Turner, C., Anderson, C., Blomquist, P., Simons, D., ... & Lamagni, T. (2022). Comparative transmission of SARS-CoV-2 Omicron (B. 1.1. 529) and Delta (B. 1.617. 2) variants and the impact of vaccination: national cohort study, England. medRxiv.



Mutated Amino Acids in RBD regions for different COVID-19 variants

* Receptor-binding domain (RBD) region is the key part of virus spike that allows the virus to dock to the body cell's receptors.

At least **15 mutations of amino acids** were observed at the RBD region of Omicron variant result in **stonger binding to human ACE-2 receptor on the cells.**

DEC 2019

SARS-CoV-2 was first identified.

WUHAN, CHINA

Alpha

DEC 2020 / UK
- ↑ Transmissibility (~50%)
- ↑ Severity
- ↑ Case Fatality

Beta

DEC 2020 / SOUTH AFRICA
- ↑ Transmissibility (~50%)
- ↓ Susceptibility to EUA monoclonal antibody treatments

Gamma

JAN 2021 / BRAZIL
- ↓ Susceptibility to bamlanivimab/etesevimab monoclonal antibody treatments

Delta

MAY 2021 / INDIA
- ↑ Transmissibility
- ↓ Susceptibility to EUA monoclonal antibody treatments

Omicron rapidly replace other variants to infect ppl

NOV 2021 / SOUTH AFRICA
- ↑ Transmissibility
- ↑ Risks of Re-Infection

Deletion in the S gene leads to the failure detection of some PCR assays.

*EUA monoclonal antibody refers to the unique monoclonal antibody that bind specifically to the SARS-CoV-2 spike protein to inhibit the ability of virus to infect human body cells. These clinical monoclonal antibodies are permitted by FDA - Emergency Use Authorization (EUA) under certain criteria, but with significantly less data, as to use for hospital-administered COVID patients.

This poster is used for informational purposes only. The content is mainly summarized from Ref [1].

Brought to You By CYTO+

Emerging COVID-19 Variants
& Their Impact on Detection, Therapeutic Strategies & Vaccination

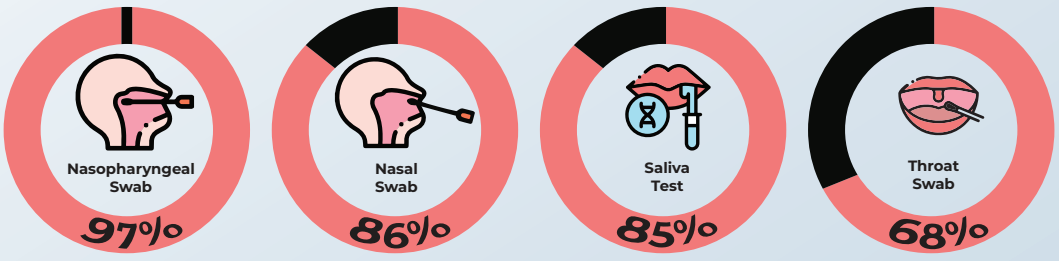
Detection

Real-time Polymerase Chain Reaction (RT-PCR) is regarded as the gold-standard laboratory technique for identification of SARS-CoV-2 in a clinical setting.

What is RT-PCR?

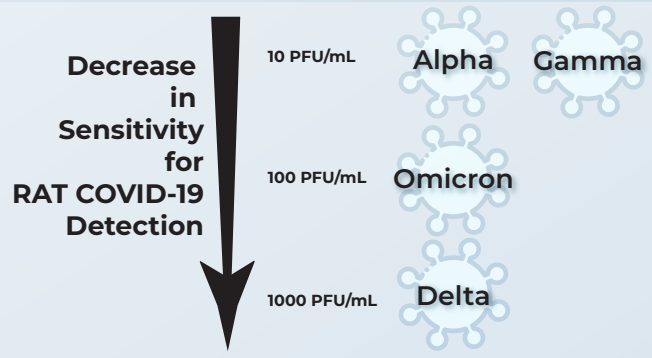
RT-PCR technology is based on **detecting the presence of specific viral RNA** belonging to the viral envelope, nucleocapsid, spike and ORF1ab regions. Therefore, viral mutations can potentially alter the accuracy of this method, leading to unpredictable test performances and false-negatives. However, this challenge could be overcome by using multi-target assays and specific primers could be used to detect different VOCs.

Sensitivity of Different RT-PCR sampling approaches



What is Rapid Antigen Test (RAT)?

Rapid antigen test is the rapid diagnostic test (specific antigen-antibody binding) used to detect the presence of antigen. The commercially available kits are mainly detect the presence of two main SARS-CoV-2 antigens (S and N proteins). However, the success rate of these assays is largely dependent on factors such as disease stage and viral load (1–3 days before to 5–7 days after the onset of symptoms).



*** PFU/mL represent the number of viruses within the samples. In this case, higher PFU/mL means a higher number of viruses are required for the detection of RAT.**

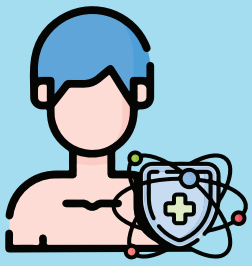
In a study [ref 5], the RAT had shown the highest sensitivity for the detection of the Alpha and Gamma variants, followed by Omicron and Delta.

Therapeutic Strategies

Anti-Viral Drugs

[To prevent the virus from multiplying]

Example: Remdesivir

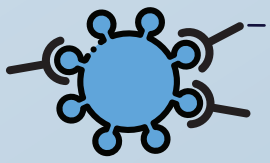


Immunomodulatory Drugs

[help the immune system to fight the virus or stop it from overreacting dangerously]

Example: Various Monoclonal Antibodies

EUA Monoclonal Antibody Treatments



Monoclonal antibodies (mAbs) that target the spike protein of SARS-CoV-2 are intervented to inhibit the binding of virus to the human cells and stop the viral infection.

Example: Monoclonal Antibody (LY-CoV016, REGN10933, AZD1061, BRII-196, etc.)

mAbs treat SARS-CoV-2 specifically. The emerging variants may escape from the binding of mAbs and reduced the efficacy. The most recent VOC, Omicron showed decreased susceptibility to neutralization for most of the monoclonal antibodies. In a report [ref 6], over 85% of the tested mAbs are escaped by Omicron.

Vaccines

Since the period of starting the COVID vaccination programme, the severe COVID cases were declining sharply and the COVID vaccines show highly effectiveness for preventing hospital admissions with COVID-19 infection. However, the vaccination efficacy show certain declines over time and when the arising of new VOCs. Authorization of 3rd vaccine dose in an effort is to maintain the effectiveness of vaccination.

The Vaccine effectiveness against symptomatic disease is manipulated by:

- **The Duration of Protection after Vaccination**
- **The Emergence of COVID Variants (Mutation of Virus)**

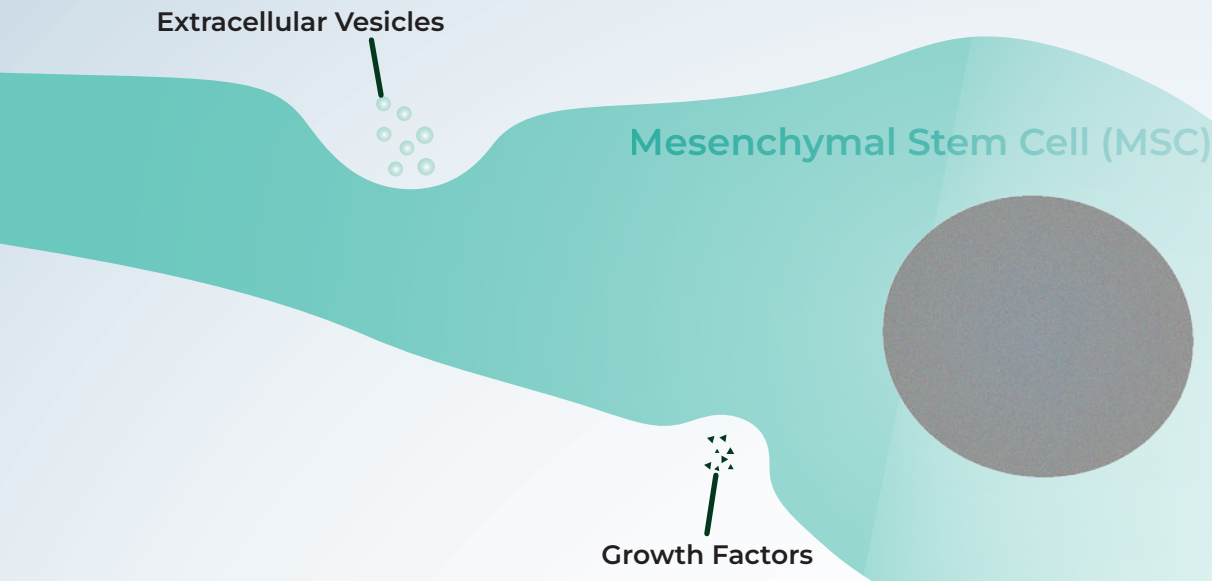
In an analysis to study the vaccine effectiveness in the UK population had resulted:

- the first two doses of ChAdOx1 nCoV-19 (AstraZeneca) or BNT162b2 (Pfizer-BioNTech) had shown **a limited protection against symptomatic disease caused by the Omicron variant.** The protection even declined over time to less than 10% after 20 weeks of vaccination.
- a booster of either BNT162b2 or mRNA-1273 (Moderna) substaintially increased protection even the protection waned over time.

This poster is used for informational purposes only.

Brought to You By CYTO+

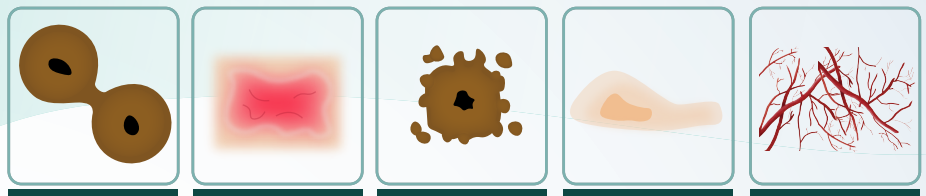
Therapeutic Potentials of Mesenchymal Stem Cells in Multiple Organs Affected by COVID-19



MSC Paracrine Effect

MSC secretes biologically active molecules that exert beneficial effects on injured tissues

The effects include:



Lungs

The lungs are the most affected organs by SARS-CoV-2 infection.

Effects of COVID-19 Infection

- Diffuse alveolar injury
- Hyaline membrane formation
- Alveolar edema and infiltration
- Progressive loss of function
- Pulmonary fibrosis

MSC Therapeutic Potential

- ↓ Viral load
- ↓ Epithelial cell apoptosis
- ↑ Alveolar fluid clearance and angiogenesis
- ↓ Pulmonary fibrosis
- Alveolar epithelial integrity recovery

Blood Vessels

COVID-19 seems to cause more frequent thrombotic disorders or endothelial damage than infections by other respiratory viruses.

Effects of COVID-19 Infection

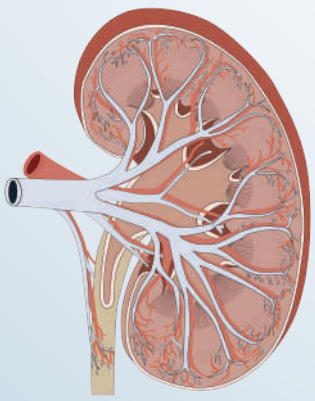
- Endothelial cell infection
- Hyperperfusion of inefficient alveoli
- Procoagulant profile
- ↑ Thrombotic disorder

MSC Therapeutic Potential

- ↓ Endothelial cell apoptosis
- ↓ Lung endothelial barrier permeability
- ↑ Angiogenesis
- Perserve endothelial barrier function

Kidneys

Findings show SARS-CoV-2 can directly infect renal epithelia, promoting renal acute injury in patient with COVID-19.



Effects of COVID-19 Infection

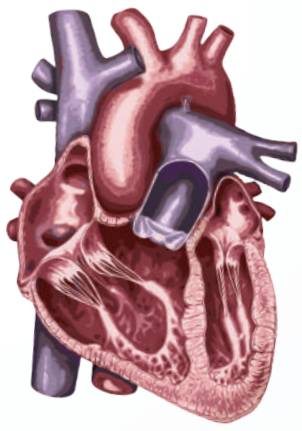
- Tubular injury
- Necrotic lesions
- Epithelium detachment
- Bowman's capsule rupture
- Renal dysfunction

MSC Therapeutic Potential

- ↓ Tubular cell apoptosis
- ↓ Inflammatory infiltrate
- Nephroprotective effects
- Regeneration of renal tubular cells through MSC-derived extravascular vesicles

Heart

COVID-19 patients without previous history of cardiovascular disease displayed cardiovascular manifestations in addition to clinical symptoms.



Effects of COVID-19 Infection

- Myocardiditis (inflammation of heart muscle)/ myocardial injury
- Hypoxia
- Myocardium fibrosis
- Acute cardiac injury with several COVID-19 related cardiac implications

MSC Therapeutic Potential

- ↑ Myocardial contractility (innate ability of heart muscle to contract)
- ↓ Apoptosis ↓Oxidative stress
- Preserve cardiac function
- ↓ Fibrosis

Central Nervous System

Parts of COVID-19 patients developed mild to severe neurological events.

Effects of COVID-19 Infection

- Severe neurological symptoms (acute ischemic stroke, cerebral venous sinus thrombosis, cerebral hemorrhage)
- Neuron degeneration
- Ischemic brain injury
- Mild neuro-inflammation to hypoxia

MSC Therapeutic Potential

- ↑ Neuro-protective effect against cytotoxicity
- ↑ Neurovascular recovery and plasticity
- ↑ miR-133b to promote neuron growth
- ↑ Blood-brain barrier integrity ↑angiogenesis

REFERENCES

[1] Fernandes, Q., Inchakalody, V. P., Merhi, M., Mestiri, S., Taib, N., Moustafa Abo El-Ella, D., ... & Dermime, S. (2022). Emerging COVID-19 variants and their impact on SARS-CoV-2 diagnosis, therapeutics and vaccines. Annals of Medicine, 54(1), 524-540.
[2] Tsang, N. N. Y., So, H. C., Ng, K. Y., Cowling, B. J., Leung, G. M., & Ip, D. K. M. (2021). Diagnostic performance of different sampling approaches for SARS-CoV-2 RT-PCR testing: a systematic review and meta-analysis. The Lancet Infectious Diseases, 21(9), 1233-1245.
[3] World Health Organization (WHO). (n.d.). Tracking SARS-CoV-2 variants. Retrieved from https://www.who.int/en/activities/tracking-SARS-CoV-2-variants/, at 9th March 2022.
[4] Allen, H., Tessier, E., Turner, C., Anderson, C., Blomquist, P., Simons, D., ... & Lamagni, T. (2022). Comparative transmission of SARS-CoV-2 Omicron (B. 1.1. 529) and Delta (B. 1.617. 2) variants and the impact of vaccination: national cohort study, England. medRxiv.
[5] Salcedo, N., Nandu, N., Boucau, J., & Herrera, B. B. (2022). Detection of SARS-CoV-2 Omicron, Delta, Alpha and Gamma variants using a rapid antigen test. medRxiv.
[6] Cao, Y. R., Wang, J., Jian, F., Xiao, T., Song, W., Yisimayi, A., ... & Xie, X. S. (2021). B. 1.1. 529 escapes the majority of SARS-CoV-2 neutralizing antibodies of diverse epitopes. BioRxiv.
[7] Lauring, A. S., Tenforde, M. W., Chappell, J. D., Gaglani, M., Ginde, A. A., McNeal, T., ... & Self, W. H. (2022). Clinical severity of, and effectiveness of mRNA vaccines against, covid-19 from omicron, delta, and alpha SARS-CoV-2 variants in the United States: prospective observational study. bmj, 376.
[8] Andrews, N., Stowe, J., Kirsebom, F., Toffa, S., Rickeard, T., Gallagher, E., ... & Lopez Bernal, J. (2022). Covid-19 vaccine effectiveness against the omicron (B. 1.1. 529) variant. New England Journal of Medicine.
[9] Paris, G. C., Azevedo, A. A., Ferreira, A. L., Azevedo, Y. M., Rainho, M. A., Oliveira, G. P., ... & Thole, A. A. (2021). Therapeutic potential of mesenchymal stem cells in multiple organs affected by COVID-19. Life Sciences, 278, 119510.

This poster is used for informational purposes only.

Brought to You By CYTO+