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Monoclonal Antibodies Against SARS-CoV-2 Variants

Although the world has returned to a state of relative normalcy, SARS-CoV-2 infections continue to persist worldwide, and immune evasive variants continue to emerge. Monoclonal antibodies (mAbs) are often first in line therapy for SARS-CoV-2 infections, but most have lost utility against the Omicron variant and its subvariants. One mAb cocktail, Evusheld, composed of Tixagevimab and Colgavimab, has retained neutralizing capacity against currently circulating variants of Omicron. However, Evusheld is mammalian-made and as such has the risk of antibody-dependent enhancement (ADE) of infection.

Researchers at the Biodesign Institute of Arizona State University have used glycoengineering to make new versions of Tixagevimab and Cilgavimab, termed pTixagevimab and pCilgavimab, in Nicotiana benthamiana. The plant-made counterparts of these mAbs are able to efficiently neutralize multiple omicron subvariants of SARS-CoV-2, including BA.5 and BA.4.6 and may have enhanced effector function. The variable regions of Tixagevimab and Cilgavimab were genetically fused onto a human IgG1 backbone, without the mutations that eliminate the Fc receptor binding of Evusheld mAbs. They were then transiently expressed in transgenic N. benthamiana plants. Glycan analysis showed that both mAbs contain highly homogeneous N-linked glycans with >95% carrying human-like biantennary GnGn or hybrid MGn glycoforms. Plant based production may allow for a more consistent therapeutic mAb product.

This technology provides plant-produced anti-SARS-CoV-2 mAbs with restored Fc receptor binding and effector function and enhanced ADCC activity with no risk of ADE.

Potential Applications

- Plant-based production of pCilgavimab and pTixagevimab
  - Treatment of SARS-CoV-2 infections, including infections arising from Omicron variants

Benefits and Advantages

- These mAbs specifically recognized the RBD of SARS-CoV-2 and were able to neutralize the authentic parental Omicron variant (B.1.1.529) in a foci-forming assay, with an IC50 of 2.23 lg/mL and 19.68 lg/mL, respectively
- Glycoengineerd to restore Fc receptor binding and effector function
  - No side effect risks, such as ADE
  - Greater efficacy
  - Compared to the parent mAbs, pCilgavimab and pTixagevimab restored the FcγR binding and contained highly homogeneous, human-like glycans
- GnGn glycoform enhanced ADCC activity (greater potency)
- Effective against most known SARS-CoV-2 Variants
- High transient expression levels (up to 403-726 mg/kg FLW)

For more information about this opportunity, please see

Jugler et al - Plant Biotechnol J - 2023

For more information about the inventor(s) and their research, please see

Dr. Chen's departmental webpage