I BEST OF THE WEEK (05 nov – 11 dic 2022)

Arevalo C.P et al.

A multivalent nucleoside-modified mRNA vaccine against all known influenza virus subtypes

Science, November 2022; doi/10.1126/science.abm0271

Abstract

Seasonal influenza vaccines offer little protection against pandemic influenza virus strains. It is difficult to create effective prepandemic vaccines because it is uncertain which influenza virus subtype will cause the next pandemic. In this work, we developed a nucleoside-modified messenger RNA (mRNA)–lipid nanoparticle vaccine encoding hemagglutinin antigens from all 20 known influenza A virussubtypes and influenza B virus lineages. This multivalent vaccine elicited high levels of cross-reactiveand subtype-specific antibodies in mice and ferrets that reacted to all 20 encoded antigens.Vaccination protected mice and ferrets challenged with matched and mismatched viral strains, and this protection was at least partially dependent on antibodies. Our studies indicate that mRNA vaccines can provide protection against antigenically variable viruses by simultaneously inducing antibodies against multiple antigens.

Prerna Arora et al.

The effect of cilgavimab and neutralisation by vaccine-induced antibodies in emerging SARSCoV-2 BA.4 and BA.5 sublineages

The Lancet, October 2022; doi.org/10.1016/S1473-3099(22)00693-4

Abstract

Since the first detection of the SARS-CoV-2 omicron variant (B.1.1.529 and sublineages) in November 2021 in South Africa, Botswana, and Hong Kong, several omicron sublineages have evolved. Some of these sublineages, including BA.2.75, BA.4, and BA.5, have shown augmented resistance against antibody-mediated neutralisation Thus, these sublineages outcompete earlier Omicron sublineages in populations with pre-existing immune responses due to either infection, or vaccination, or both.

Our data indicate that emerging BA.4 and BA.5 sublineages harbouring S-protein mutations (R346T,
R346S, or R346S) have further extended their capacity to evade neutralisation. As a consequence, the availability of therapeutic antibodies for the treatment of individuals infected with such viruses is further reduced, and infections in triple-vaccinated individuals might become increasingly frequent.

Qian Wang et al.

Resistance of SARS-CoV-2 omicron subvariant BA.4.6 to antibody neutralisation

The Lancet, October 2022; doi.org/10.1016/S1473-3099(22)00694-6

Abstract
SARS-CoV-2, the causative agent of the COVID-19 pandemic, continues to evolve. A subvariant of SARS-CoV-2 omicron (B.1.1.529), known as BA.4.6, emerged in March, 2022, and it appears to be expanding its coverage even in the presence of BA.5, the globally dominant subvariant in recent months (appendix p 2).1, 2 Compared with subvariants BA.4 and BA.5 (hereafter referred to as BA.4/5), BA.4.6 contains two additional mutations, R346T and N658S, in the spike protein (appendix p 2). Three other nascent omicron subvariants with similar spike mutations, BA.4.7 with R346S, BA.5.9 with R346I, and BF.7 with R346T, have also been detected, although at very low frequencies (appendixp 2). The fact that these four new subvariants all have mutations at the R346 residue raises concerns for further antibody evasion, because R346K in a previous subvariant of omicron (BA.1.1) impaired the potency of several therapeutic monoclonal antibodies (mAbs).
The combination of cilgavimab and tixagevimab, which had received emergency use authorisation for the prevention of COVID-19,5 could not neutralise BA.4.6, BA.4.7, BA.5.9, or BF.7, nor the authentic BA.4.6 (appendix p 6).
The loss of thisantibody combination against BA.4.6 leaves bebtelovimab as the only therapeutic mAb that retained potent activity against all circulating forms of SARS-CoV-2. As the COVID-19 pandemic and SARS-CoV-2 continue to evolve, our arsenal of authorised monoclonal antibodies might soon be depleted, thereby jeopardising the wellbeing of millions of immunocompromised individuals who cannot robustly respond to COVID-19 vaccines.

Amjadi M. F et al.
Anti-membrane Antibodies Persist at Least One Year and Discriminate Between Past Coronavirus Disease 2019 Infection and Vaccination
The journal of Infectious Diseases¸ June 2022; doi.org/10.1093/infdis/jiac263
Abstract
Background
The consequences of past coronavirus disease 2019 (COVID-19) infection for personal and population health are emerging, but accurately identifying distant infection is a challenge. Anti-spike antibodies rise after both vaccination and infection and anti-nucleocapsid antibodies rapidly decline.
Methods
We evaluated anti-membrane antibodies in COVID-19 naive, vaccinated, and convalescent subjects to determine if they persist and accurately detect distant infection.
Results
We found that anti-membrane antibodies persist for at least 1 year and are a sensitive and specific marker of past COVID-19 infection.
Conclusions
Thus, anti-membrane and anti-spike antibodies together can differentiate between COVID-19 convalescent, vaccinated, and naive states to advance public health and research.