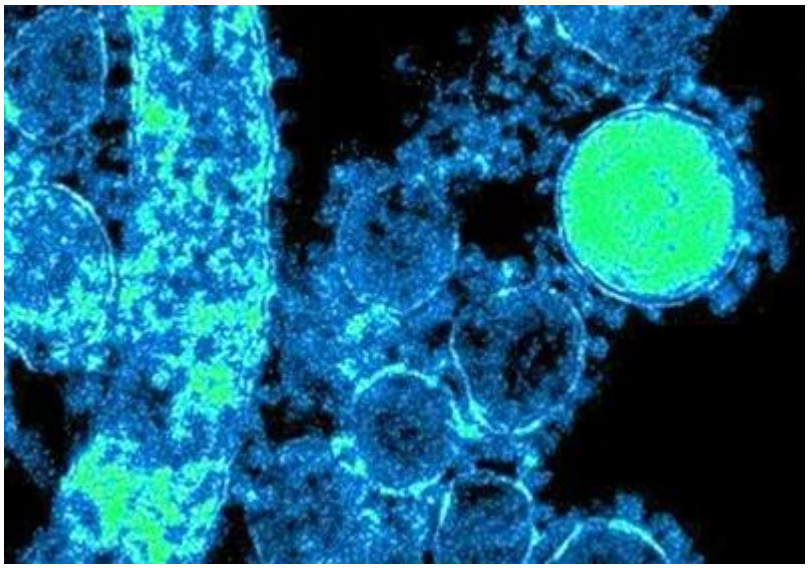
BNT162b2 (Pfizer- BioNTech) and mRNA 1273 (Moderna) vaccines were the first messenger RNA (mRNA)-based vaccines ever approved. In both vaccines, an mRNA sequence determines the structure and assembly of the immunogen, the SARS-CoV-2 spike (S) glycoprotein. In this study, the authors from Italy and the United Kingdom used mass spectrometry analysis to investigate the presence of recombinant S protein, encoded by the mRNA vaccine, in blood samples of participants vaccinated with mRNA COVID-19 vaccines.

The researchers emphasized that synthetic and natural SARS-CoV-2 S proteins can be distinguished because they produce different tryptic digestion products. When digested by an enzyme, trypsin, the wild-type SAR-CoV-2 protein produces two smaller fragments, namely LDK + VEAEVQIDR. The recombinant SARS-CoV-2 S protein encoded by the mRNA vaccine produces an LDPPEAEVQIDR fragment (PP-spike marker).

The S protein appears to be a major pathogenic factor that contributes to the unique pathogenesis of SARS-CoV-2. The S protein plays three critical roles in facilitating host cell entry: it must bind to the host cell angiotensin-converting enzyme 2 receptor (ACE2), be proteolytically processed, and promote membrane fusion. Because of these reasons, it is one of the most important targets for vaccine development and therapeutic approaches against COVID-19. On the other hand, numerous studies have shown that the S protein by itself, without the rest of the viral components, is sufficient to promote various pathological effects and cause damage to different cells and organs.



About the study

The study included 60 individuals: 20 vaccinated against COVID-19 who received the full cycle of the mRNA vaccine and 40 unvaccinated controls (20 tested negative for COVID-19 and 20 tested positive for COVID-19). Mass spectrometry was used to detect specific fragments of recombinant S protein encoded by the mRNA vaccine (in this study called PP-spike) in biological samples.

The results showed that approximately 50% of individuals who received mRNA-based COVID-19 vaccines had specific fragments of recombinant S protein in their blood samples. The minimum time when the PP-spike fragment was detected was 69 days after vaccination, and the maximum time was 187 days after vaccination.

The presence of circulating recombinant S protein was independent of the anti-SARS-CoV-2 IgG antibody titer.

All samples from 40 unvaccinated individuals (tested negative or positive for COVID-19) were negative for recombinant S protein.

Based on these results, the authors proposed several possible molecular mechanisms responsible for the persistence of the "PP spike fragment"- Figure 1.

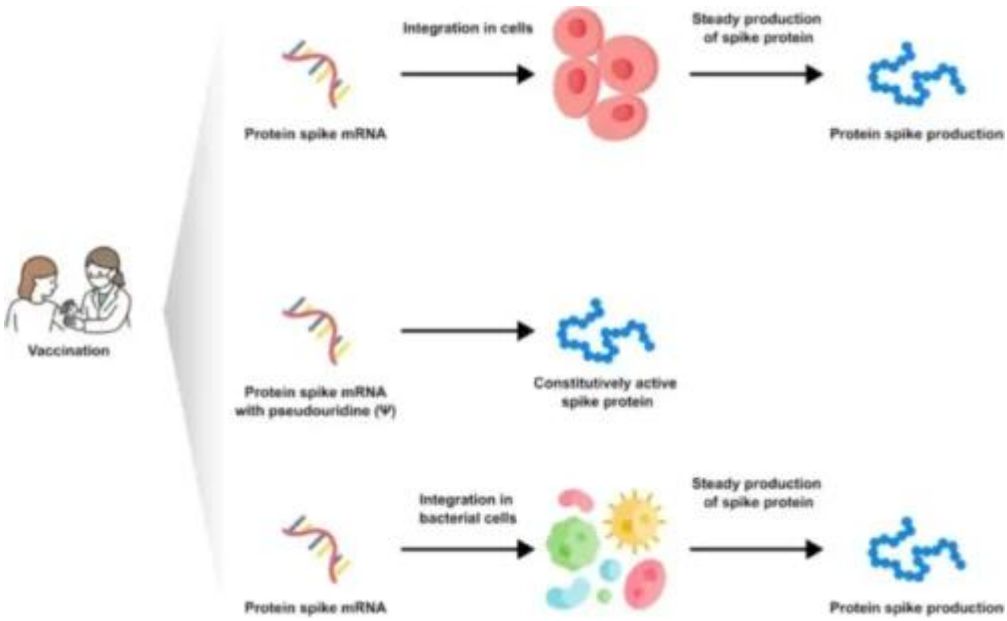


Figure 1 from the article by Brogna C et al. Proteomics Clin. Appl. 2023

Conclusion

This mass spectrometry analysis demonstrated that approximately 50% of those vaccinated against COVID-19 had specific fragments of recombinant S protein in their blood samples 2-6 months after vaccination. All blood samples from unvaccinated controls were negative for the presence of recombinant S protein.

The authors emphasized that this mass spectrometry analysis is the first proteomic detection of recombinant S protein in subjects who had been vaccinated. The results confirmed that this method allows the detection of circulating S protein encoded by an mRNA vaccine, and the evaluation of its half-life.

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Journal Reference

Brogna C, Cristoni S et al. Detection of recombinant Spike protein in the blood of individuals vaccinated against SARS-CoV-2: Possible molecular mechanisms. Proteomics Clin. Appl. 2023; 2300048. (Open Access) https://doi.org/10.1002/prca.202300048