The authors from Italy and the United Kingdom used proteomic approach to investigate the presence of recombinant spike (S) protein, encoded by the mRNA vaccine in blood samples from participants vaccinated with anti-SARS-CoV-2 mRNA vaccine and unvaccinated participants who tested negative or positive for COVID-19. Mass spectrometry analysis showed that approximately 50% of subjects who received mRNA-based vaccines had specific fragments of recombinant S protein in their blood samples 2-6 months after vaccination. All blood samples from individuals who were not vaccinated were negative for recombinant S protein.

Glycosylated S protein is one of the four major proteins of SARS-CoV-2. It enables recognition of the host cell receptor and subsequent viral entry into the host cell. Because of these reasons, it is one of the most important targets for the developing of vaccines and therapeutic approaches against COVID-19. The two most widely used vaccine products composed of mRNA filaments encapsulated in lipid nanoparticles are Pfizer-BioNTech (BNT162b2- Comirnaty) and Moderna (mRNA-1273). Both mRNA vaccines encode the same recombinant S protein, which differs from the wild-type protein by specific amino acid changes at positions 986 and 987 (K986P and V987P), i.e., the amino acids lysine and valine are both replaced by two proline amino acids to stabilize the S protein conformation in an inactive prefusion state.

The researchers emphasized that it is possible to distinguish synthetic and natural S proteins 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, whereas the recombinant S protein encoded by the mRNA vaccine produces an LDPPEAEVQIDR fragment (PP-spike marker). The introducion of the double amino acid variation abolishes a tryptic digestion site.

Previous study has also shown the presence of circulating S protein in plasma samples from approximately 6o% of patients with postacute sequelae of coronavirus disease (PASC) at some time point up to 12 months after diagnosis of SARS-CoV-2 infection. In addition, S1 was detected in approximately 20% of PASC patients, whereas N was detected in one patient at multiple time points. Importantly, the S protein was not found in plasma samples of participants who were not diagnosed with PASC after they had suffered from COVID-19. https://discovermednews.com/the-presence-of-circulating-spike-protein-in-vaccinated-and-unvaccinated-patients-with-symptoms-of-postacute-covid/

About the study

The study included 60 subjects, 20 of whom were vaccinated with the full cycle of mRNA vaccine. There were two control groups: 20 unvaccinated subjects who tested negative for COVID-19 and had no antibodies detected, and 20 unvaccinated subjects who tested positive for COVID-19. The presence of specific fragments of recombinant S protein (in this study called PP-spike) in biological samples was detected by mass spectrometry.

A mass spectrometry analysis of blood samples showed that approximately 50% of subjects who received mRNA-based vaccines had specific fragments of recombinant S protein. The presence of recombinant S protein was independent of the anti-SARS-CoV-2 IgG antibody titer. The minimum time when PP-S fragment was detected was 69 days after vaccination, whereas the maximum time was 187 days.

Recombinant S protein was negative in all samples from 20 unvaccinated individuals who tested negative for COVID-19, as well as the samples from 20 unvaccinated people who were positive for COVID-19.

Based on these results, the authors proposed three possible molecular mechanisms for the persistence of the “PP spike fragment”. First, the mRNA can be integrated or re-transcribed in certain cells, second, pseudo-uridines at a specific sequence position induce the formation of the S protein, which is always constitutively active. Third, nanoparticles containing the mRNA are taken up by the blood microbiota, which is normally present in the blood at the basal level.

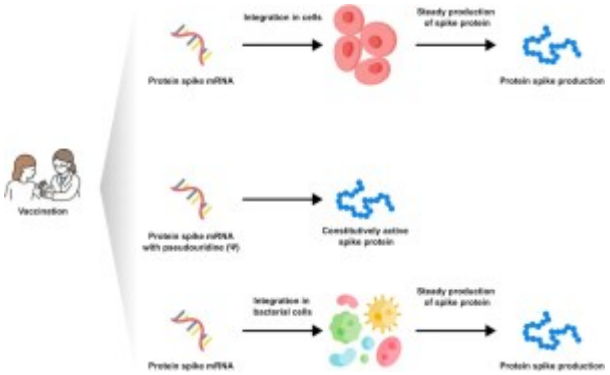

Figure from the original article by Brogna C et al. Proteomics Clin. Appl. 2023

In conclusion, mass spectrometry examination of blood samples has shown that approximately 50% of subjects who received mRNA-based vaccines had specific fragments of recombinant S protein in their blood samples 2-6 months after vaccination. This is the first proteomic detection of recombinant S protein in subjects who had been vaccinated. The recombinant S protein in vaccinated individuals was found two to six months after the vaccination.

This study has shown that this method allows the detection of circulating S protein encoded by an mRNA vaccine, and the evaluation of the half-life of the recombinant S protein. The authors claim that this method allows weighing the potential risks and benefits of further booster doses of SARS-CoV-2 mRNA vaccine.

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