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Advantages of an Oral Vaccine to Control the COVID-19 Pandemic

Although vaccines are essential for controlling pandemics, the procedures used to manufacture and deliver them for worldwide use are often extremely difficult to implement in many less-developed countries in a timely manner—if at all. Indeed, the technology exists to isolate and sequence mRNA that codes for the synthesis of critical viral antigens. In the case of coronavirus disease 2019 (COVID-19), vaccinating with a mRNA-based vaccine causes human muscle cells to make viral spike protein that stimulates the host immune system to make protective antibodies specific for that antigen. This is now being done using several mRNA vaccines authorized by the Food and Drug Administration for emergency use in humans. Unfortunately, such vaccines require a sophisticated manufacturing process, a costly cold chain to preserve and maintain vaccine potency, large supplies of sterile vials, needles, and surgical gloves, as well as large numbers of trained vaccinators to administer to millions of people. These are major obstacles to achieving the degree of “herd immunity” desired to contain a pandemic in countries without such resources and technology.

The development and use of an oral vaccine against COVID-19 would be a better alternative to generate widespread immunity for those living in remote areas or less-developed countries. It would consist of inserting the gene that encodes for the COVID-19 spike protein into a harmless bacterium (eg, *Lactobacillus plantarum*) commonly found in yogurt or other foodstuffs. Once ingested, this bacterial construct would populate the intestinal flora where it would produce large amounts of viral spike protein to stimulate the host mucosal immune system—the largest collection of immune cells in the body—to make significant amounts of protective antibody specific for the spike protein. This would not require the use of an adjuvant or any other agent to augment the magnitude of the antibody

response. In fact, an oral vaccine to prevent the transmission of Lyme disease already has been developed; there is much evidence to indicate that it is both safe and effective when tested in animal models of infection.¹

An oral vaccine against COVID-19 offers many advantages over the parenterally administered mRNA vaccines now being used, even though these vaccines certainly have been found to be both effective and safe. An oral vaccine could be manufactured and inexpensively delivered to any place in the world—without the need for a sophisticated manufacturing facility, an expensive cold chain for storage, trained vaccinators, and so on—in the form of a food (eg, yogurt), or as a lyophilized, temperature stable, probiotic pill.

The efficacy and the degree of protective immunity induced by an oral vaccine could easily be assessed by monitoring the presence of the bacterial construct in stool specimens, as well as determining the levels of protective antibodies present in serum at various intervals after ingestion. If there is a decline in either, one could simply ingest more vaccine. More important, such a vaccine could be modified easily in response to the emergence of new viral variants by simply adding new bacterial constructs, thereby preventing the occurrence of worldwide waves of new infections. It also should be noted that because of its Generally Recognized as Safe (GRAS) status as a natural component of a food, an oral *Lactobacillus* vaccine would have more appeal to the public and require less stringent proof of safety by the Food and Drug Administration for approval as a human vaccine.

Controlling the COVID-19 pandemic requires a global effort because the appearance of new waves of infection caused by the emergence of genetic variants in 1 country can spread rapidly to other countries. Obviously, the ability to add new bacterial constructs to an existing oral vaccine is an important attribute and provides an excellent way to stay “ahead of the curve” to moderate, if not prevent, the occurrence of such new waves of infection.

In brief, the development of an oral vaccine against COVID-19 is feasible and the need is urgent. We certainly have both the talent and technological expertise to realize such a goal.

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Reference

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