Science with Dr. Doug

Will an RNA Vaccine Permanently Alter My DNA?

Dr. Doug November 27, 2020 COVID-19, vaccine
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When people hear the words RNA vaccine, the first question that comes to the average person's mind is, "Will this vaccine permanently alter my DNA?" The second question is, "If the vaccine does alter my DNA, what are the potential long-term health impacts?"

These are fair questions. Unfortunately, these questions are usually brushed aside, ignored, minimized, or discounted by the pharmaceutical ecosystem. This concern about genetic modification is normally answered by the following argument: RNA will not permanently alter your DNA because it is a temporary molecule that quickly becomes destroyed in the cell, and because it is fundamentally different than DNA. RNA does not integrate into DNA, and RNA doesn't remain in the cell permanently because the cell destroys the RNA relatively quickly. Therefore, there is no potential risk of an RNA vaccine genetically modifying a person's genome.

On the surface, this seems like a rock-solid answer. It is the textbook response that would earn a 100% grade on an examination for a college-level molecular biology class.

However, the cells in our body know nothing of the exams being taken by graduate students.

First, let me briefly describe how an RNA vaccine works. Second, let me show you viable cellular pathways where an RNA vaccine could make its way into someone's permanent genetic material.

An RNA vaccine works by turning a small portion of the cells in our body into a vaccine production factory. Both RNA and DNA are information carrying molecules. They carry instructions on how to build specific proteins. Our cells read this information, and then build proteins according to the instructions. In the case of an RNA vaccine, the delivered RNA instructions instruct our cells to build a near-perfect replica of a very specific protein that resides on the outside of the SARS-CoV-2 virus called the "Spike" protein. This Spike protein normally resides on the outside of the virus and functions as a tether that enables the virus to

enter into a human cell. Because the Spike Protein resides on the outside of the virus, it's prime real estate for our immune system to target.

Therefore, when you are administered an RNA vaccine, this RNA will enter a small portion of your cells, and these cells will start churning out a replica of the viral Spike protein. It's important to realize that your cells are not producing the entire virus, just a portion of the virus — the Spike protein. Because it is foreign to the body, this cellularly produced Spike protein will then prompt your immune cells to learn how to develop antibodies that specifically recognize the Spike protein. At this point, you are "vaccinated" because you have acquired antibodies that recognize the virus (via the Spike protein), as well as memory cells that can produce more of the antibody should you be infected with the actual virus. If your body is exposed to the coronavirus, these antibodies will recognize the Spike protein on the outside of the virus. When the virus is coated in antibodies, it is "neutralized" and can no longer infect other cells.

Most other vaccines work by administering the Spike protein directly into your body, or by introducing an attenuated or inactivated virus that contains the Spike protein. In these types of traditional vaccines, the Spike protein was previously made in a vaccine production facility. In an RNA vaccine, there is no Spike protein in the vaccine. Instead, the vaccine provides your cells with instructions on how to build the Spike protein. Essentially, your cells have become the vaccine production factory. After some time, this delivered RNA will be destroyed by our cells, and the cells will stop producing the Spike protein. Our body should be left unchanged, except for the presence of antibodies and immune cells which now recognize the Spike protein of the virus.

In theory, this is how the vaccine should work. Sounds great on paper, doesn't it?

Before jumping to reductionist conclusions, let's go one level deeper into molecular biology to answer the question of whether or not this extraneous RNA could potentially alter our DNA permanently. I believe the answer to this question is yes.

It is well known that RNA can be "reverse transcribed" into DNA. Residing in our cells are enzymes called "reverse transcriptases". These enzymes convert RNA into DNA. Multiple sources for this class of enzymes exist within our cells. These reverse transcriptases are normally made by other viruses termed "retroviruses". HIV is a retrovirus and so is Hepatitis B, but there are many other retroviruses that fall in this category. In addition to these external viruses, there are viruses that are hard-wired into our genomic DNA called endogenous retroviruses (ERVs). These ERVs harbor instructions to produce reverse transcriptase. In addition to ERVs, there are mobile genetic elements residing in our DNA called LTR-retrotransposons that also encode for reverse transcriptase enzymes. To top it all off, reverse transcriptase is naturally used by our cells to extend the telomeres at the end of chromosomes.

These endogenous reverse transcriptase enzymes can essentially take single-stranded RNA and convert it into double-stranded DNA. This DNA can then be integrated into the DNA in the nucleus through an enzyme termed DNA integrase.

With so many sources of reverse transcriptase, it is quite probable that the RNA introduced into our cells via the vaccine could be reverse transcribed into a segment of double-stranded DNA, and then integrated into our core genetic material in the nucleus of the cell. A variety of specific conditions need to be present for this to occur, but it is possible if the right convergence occurs. Biology is messy and not always perfectly predictable, even when the "rules" are known *a priori*.

Even though the initial vaccine is only introduced into a relatively small portion of our cells, if this reverse transcription process occurs in stem cells, then this genetically modified cell can be replicated and amplified to a larger portion of cells that make up the tissues of the body. Stem cells serve as a reservoir to produce new cells in perpetual fashion. In this way, over time, a larger percentage of our somatic cells can be replaced by these genetically modified stem-cell precursors. This type of genetically modified replacement of cells is seen in some patients who have received bone-marrow transplants from other patients. In these patients, even germline cells such as sperm can inherit these genetic modifications, even though the pathway for this germline modification is still not understood. In these patients, the so called "rules" that presumably prevented such an outcome were violated.

I think most molecular biologists would look at my thesis and discount it as improbable, and I wouldn't argue with them too strongly. After all, if these reverse pathways from RNA to DNA were actively possible, wouldn't a normal infection by the virus cause the same problem? Wouldn't the RNA introduced by a viral infection of SARS-CoV-2 serve as a potential substrate for permanent genetic modification of cellular DNA, just like the RNA in the vaccine?

I would answer that this possibility exists, too. However, I believe the probability of viral RNA undergoing this process is much smaller for several reasons. First, the viral RNA is packaged into viral particles which act like a shell. These RNA molecules are temporarily unpackaged from this shell while inside the cell to produce more viral RNA and viral proteins, which are quickly sequestered and repackaged into new viral particles. Also, viral RNA is inherently unstable due to sequence specific peculiarities unique to viral RNA, and is quickly recognized by cellular enzymes for destruction.

Therefore, the amount of time available for reverse transcriptase to work on "bare" viral RNA is very low. In contrast to this, the RNA provided to cells via a vaccine has been altered in the lab to increase its stability such that it persists in the cell for a much longer time. A number of modifications are made to increase the stability and longevity of this vaccine-delivered RNA. This artificial engineering of RNA is designed to produce RNA that hangs around in the cell

much longer than viral RNA, or even RNA that our cell normally produces for normal protein production. The purpose of this engineered longevity is to increase the production of Spike protein by our cells to maximize the efficacy of the vaccine. In addition, this RNA is not rapidly sequestered away into new viral particles. Therefore, the probability that a molecular pathway could be found that results in this RNA being converted over into DNA is much higher, in my opinion.

This probability may be miniscule, and may not even be noticeable in in vitro experiments, or even in clinical trials across tens of thousands of patients. The odds of this occurring may be 1 in 1 followed by many zeros; however, that miniscule probability flies out the window when you understand that the average human body has 30 trillion cells, and the vaccine will be deployed in up to 7 billion people. If you multiply these small probabilities across these large numbers, the probability that this could occur in a modestly large number of people is very real.

What happens if this occurs? There are two possible outcomes that are not mutually exclusive. First, modification of somatic cells, and in particular, stem cells, could result in a segment of the population with an increasing percentage of their tissues being converted over to genetically modified cells. These genetically modified cells will possess the genetic sequence to produce Spike Protein. Because Spike protein is a foreign protein to the human body, the immune systems of these individuals will attack the cells in their body which express this protein. These people will almost inevitably develop autoimmune conditions which are irreversible, since this foreign protein antigen is now permanently hardwired into the instructions contained in their DNA.

The second possibility is based on a pathway being found that transfers this genetic modification to germline cells (egg and sperm). This is certainly a more remote possibility, but if it occurred, this insertional genetic mutation would find itself in all future generations stemming from this individual or individuals. Because this is a germline modification and not a somatic modification, this new genetic element will be present in every single cell of these individuals. This means that potentially every tissue in their body could express Spike protein. Because this protein is present from birth, the immune system will recognize this new protein as “self” rather than non-self (foreign). If these individuals are infected with coronavirus, their immune system would fail to recognize the Spike protein of the virus as foreign, and these individuals will have substantially reduced capacity to fend off the coronavirus. Therefore, over time over future generations, a growing percentage of the population would be more susceptible to severe infection by the coronavirus due to limited immune function.

Now, none of the scenarios outlined above touch on the downstream risk of developing antibody dependent enhancement (ADE), which is a major problem with any vaccine developed for coronaviruses. ADE is a risk for any type of vaccine, including RNA vaccines. The current RNA vaccines being rushed forward have only been tested for a few months, and

ADE would not rear its ugly head for several years, although it could occur sooner. Therefore, the current clinical trial data is not anywhere close to being sufficient to rule out the health risk of ADE. If ADE does occur in an individual, then their response to the virus could be fatal when they are actually exposed to the virus post-vaccination. To learn more about the possibility of ADE, click here to read my article —> **"Is A Coronavirus Vaccine a Ticking Timebomb."**

In addition to the risks mentioned above, another risk becomes apparent: If the cell is infected with either an external virus, or endogenous retrovirus, while the vaccine is active in the cell, this from the vaccine could be genetically spliced into the existing genome of another virus. This virus would then gain a functional Spike protein, which would then allow it to infect respiratory tissues and other organs of the body. This means that viruses that were normally isolated to certain tissues would suddenly gain the ability to infect a much wider range of tissues, making them more pathogenic or deadly.

It's probably good to point out at this stage of the discussion that an RNA vaccine has never been approved for use in humans. This would be the first time in history that such an approach would be used on a massive scale. Approximately 50 clinical trials have been conducted on RNA vaccines for cancer treatment, and about a dozen RNA-based vaccines are under development for SARS-CoV-2. Two candidates, one from Pfizer/BioNTech (BNT162b2) and the other from Moderna (mRNA-1273), are the furthest along, and have shown decent efficacy in Phase III clinical trials (although I would argue strongly the sample sizes of infected individuals in both experiments were so small that making this efficacy claim is rather dubious at this stage). If you have read the news lately, these vaccines are being rushed headlong to be deployed on a massive scale with little attention being paid to the potential ramifications.

My professional opinion is that since RNA vaccines are a new mode of delivering vaccines, they should be tested for 5-10 years to demonstrate that genetic modification is not a major concern. In addition, all coronavirus vaccines, regardless of type, should be tested for an equal duration to show that ADE is not a concern. It is absolutely impossible to rule out these safety concerns in less than a year.

I only share this information so people are informed and can weigh the potential risks and benefits. The bottom line is the choice is up to you; however, for people to make such an important decision, they need to possess all of the information.

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