00:01

What if I told you that the pandemic will save the lives of millions of people? It's a difficult thing to consider, given how many loved ones we've already lost. But throughout the course of human history, massive public health crises have resulted in innovation in health care and technology. For example, the Black Death gave rise to the Gutenberg press and the 1918 flu pandemic led to modern vaccine technology. The COVID-19 pandemic has and will be no different. Just look at our vaccines -- normally developed over many years, and the mRNA vaccines were deployed in a mind-blowing 11 months.

00:54

How is that even possible? It was possible because scientists have been working for many years to get us to the point where we could use mRNA quickly in an emergency situation. Specifically, we've been working on how to help mRNA with its biggest problem, which is that it doesn't normally go to the right places inside of our bodies. Fortunately, we got around that problem just in time, and I'd like to tell you about the technology that we use to do it.

01:28

When mRNA is administered, it's injected into our muscles or our bloodstream, but we actually need it to go inside of our cells. Unfortunately, mRNA is fragile, and our bodies will destroy it before it goes very far. You can think of mRNA like a glass vase that you'd like to send in the mail without a box and bubble wrap. It'll break long before it's been delivered. And without an address on the box, your postal delivery service will have no idea where to take it. And so if we're going to use mRNA as a therapeutic, it needs our help. It needs protection, and it needs to be told where to go. And that's where I come in.

02:14

For over five decades, scientists and engineers like myself have been creating the shipping materials for nucleic acid drugs, like DNA and RNA. Through trial and error, we've created packages that deliver intact vases to the wrong address; that delivered to the right address but with a broken vase; packages that get ripped apart by attacking dogs; and packages that throw out the mail carrier's back. It's taken many years to get the science right. Let me show you the result, these tiny balls of fat that we call lipid nanoparticles. Let me tell you what they are and how they work.

03:02

So first of all, "nano" just means really, really small. Think of how small a person is compared to the diameter of the earth. That's how small a nanoparticle is compared to the person. These nanoparticles are made up of several fatty molecules called lipids. Fat is an awesome packing material -- nice and bouncy. Interestingly, our cells are also surrounded by fat to keep them flexible and protected. Years ago, scientists had the idea to create lipid nanoparticles that would act like a Trojan horse. Because the lipids in the nanoparticle look similar to the membranes that surround our cells, the cells are willing to bring the nanoparticle inside, and that's when the mRNA is released into the cell. So what, exactly, are the lipids in these nanoparticles? There are four ingredients in addition to the mRNA, and I'll tell you about each one.

04:08

First, there's a lipid called a phospholipid. This is the primary ingredient in our cell membranes, which are the walls of fat that separate the insides of our cells from everything that surrounds them. Phospholipids have a head that likes water and a tail that likes other fatty things. So when you throw a bunch of phospholipids together in water, they form this beautiful structure called a lipid bilayer. Here, the heads face the inside and the outside of the cell, which is water, and the fat-loving parts of the molecule hang out together in the middle. In lipid nanoparticles, phospholipids have a similar role of keeping all of the other ingredients organized.

04:54

Second, there's a lipid called cholesterol. Why, if cholesterol has a bad reputation, would we want to use it in a therapeutic nanoparticle? It turns out that while cholesterol can be bad when it's in our bloodstream, it's actually a really good thing for our cell membranes. And that's because those phospholipids I just told you about, they are entirely too free with themselves, and they are prone to falling apart. Cholesterol is a stiff molecule that wedges itself in between the other lipids to fill in the gaps and hold them all together. It plays a similar role in our lipid nanoparticles. It provides structural support so the nanoparticles don't fall apart in between the injection and when they get into our cells.

05:48

Third, there's a lipid called an ionizable lipid. Here, "ionizable" means that when these particles are in the bloodstream, they're neutrally charged, which helps with their safety. Then they switch to a positive charge inside of our cells, which helps them release the mRNA. Ionizable lipids are special because they have to be made in the lab, and scientists around the world have tested tens of thousands of these materials to find ones that are good at delivering mRNA safely. And because they're made in the lab, they tend to be proprietary to the company that invented them. So, for example, Moderna and BioNTech, the company that partnered with Pfizer, they

discovered different ionizable lipids, and that is the only important ingredient in their COVID-19 vaccines that differ. And even then, their ionizable lipids aren't even that different, which is reassuring, because when independent groups of scientists converge on similar solutions, it's easier to trust the result.

07:03

Finally, one more ingredient. This one is a polymer called polyethylene glycol. So let's call it PEG. That's much easier. PEG is a water-loving molecule. So it surrounds the lipid nanoparticle and it holds it all together. You can think of the other three lipids as the box and the bubble wrap for the mRNA, and the PEG as the packing tape. You may have heard in the news about a tiny fraction of people that have allergic responses to the vaccine. There is some evidence that PEG could be contributing to these allergic reactions. And that's because people are routinely exposed to PEG in cosmetic and household products, and some people have already developed antibodies against PEG. But why would this happen to some people and not to others? It turns out that every person's immune system is different, and just the same way that some people are allergic to latex, other people are allergic to PEG. It's important to keep in mind, however, that PEG has had a long history of safe use as part of FDA-approved drug formulations, and these vaccine allergies could be caused by things other than PEG. More research is needed to get to the bottom of these side effects.

08:33

All right, so let's take a step back and look at our whole nanoparticle. Beautiful, right? When these ingredients all fit together nicely, the result is a deliverywoman's dream. In the case of the vaccines, after these nanoparticles get injected into our muscle, they take the mRNA into our cells. There, the mRNA acts like an instruction manual that tells our cells to make a foreign protein, in this case, the coronavirus spike protein. When our immune cells see the spike protein, they rush to protect us from it, and they teach themselves to remember it, so that they can kill it if it ever returns. As we speak, the mRNA vaccines are out there saving lives from the coronavirus. They were our first and best tool to combat this nightmare, and they are our best hope of responding swiftly to viral variance because we can keep our lipid nanoparticle packaging the same, and all we have to do is swap out the mRNA that's inside.

09:43

But here's the best part: for mRNA therapeutics, these vaccines are only the beginning. mRNA can be used to treat or cure many diseases. So in the future, we will likely have treatments for many terrible diseases, including cystic fibrosis, muscular dystrophy and sickle cell anemia. These diseases are caused by mutated proteins, and we can use mRNA to ask our cells to make the correct version of these proteins. We'll have treatments for cancer -- breast, blood, lungs --

you name it. Here, we'll use mRNA to teach our immune cells how to find and kill cancer cells. And then, if we're lucky, we'll have vaccines against some of the most deadly and feared pathogens across the globe, including malaria, Ebola and HIV. Some of these products are already in clinical trials, and the success of the COVID-19 vaccines will pave the way for future generations of these therapies.

10:59

This is how the pandemic will save the lives of millions. It catalyzed the most rapid vaccine development in history and brought to life a niche, previously unapproved form of technology. And in our desperation, we gave that technology a chance. Now we're collecting long-term safety and efficacy data from hundreds of millions of people. And with these data, interest in the technology, funding for the technology and trust in the technology will continue to grow.

11:41

Looking ahead, the packaging and delivery of mRNA to the right organs and tissues will continue to be one of the most significant challenges to implementing this technology. And so my colleagues and I are going to be busy for a very long time. Ultimately, I'm here with a message of hope. We are on the cusp of a revolution. mRNA is about to change the world forever, and it's all thanks to these fatty little balls that take this miracle medicine to exactly where it's needed.

12:19

Thank you.

12:20

(Applause)