

now many of people watching this talk by now well have had one two three or even for doses of a messenger or in a vaccine with billions of these shots now and arms it's clear that this new way of making vaccines is both remarkably safe and incredibly effective but did you know it's not the vaccine itself that's keeping you safe it's actually you because the human body has amazing powers to both prevent and cure disease by making its own medicines you just need to know what medicine to make and that's what your vaccine gave you simply a set of instructions for how to protect yourself against sars curvy to now vaccines are only the beginning as said before the advent of em are and a vaccines is heralding in an entirely new era of medicines and marinades give us the ability to not only prevent disease but also treat previously in intractable disorders but before i get to that let's talk about really what is this new way of medicines really about well it all comes down to proteins now you may think of protein as something simply something that you need to eat and important part of your diet something that's important for you to build muscle but it's not just muscle that contains protein protein makes up an incredible have a huge fraction of the incredibly complicated ecosystem that's your entire body in many ways your body functions like a large city full of myriad buildings interconnected buildings with lots of of different structures now just as the word building fails to capture the incredible variety of structures that make up any large city the generic term protein he has no clue as to of the incredible variety of molecular architectures at the molecular level like buildings proteins are not monolithic our body makes many proteins some of some like the college and and our skin that makes our skin tough but pliable like them the action and myosin on our muscles that enable us to move or our blood is full of hemoglobin ferrying oxygen around antibodies protecting us from disease and clotting factors that close up our wounds and for any of you that have ever cracked a biochemistry textbook the should look familiar this is the metabolic chart of the human body these are all of their reactions in your body that are keeping you alive and well right now and each one of those reactions is catalyzed by a different protein whose names are shown here and blue so proteins are not only what make your your body and would make up the bulk of your body they're also what make your body tick and keep you well now if we think again

about buildings the build these structures of buildings may look quite different and the end but they're all made of a limited set of building materials and how those building materials which of those building materials are used and how they are a range aged and how they're attached to one another gives the buildings their final form the same is true of proteins if we zoom down to the molecular level we can see that proteins as if we unravel their three dimensional architecture or actually just long strings of building blocks and these building blocks have different shapes and different propensities to interact with one another so it's the which building blocks are used and they order in which they are in the chain that gives a protein its three dimensional shape now here i'm only showing three proteins but creating and maintaining a healthy human requires the combined action of over a hundred thousand different types of protein and our bodies make them all thus our bodies are remarkable protein factories at the molecular level the numbers are truly mind blowing each of the thirty trillion cells and your body that's three with thirteen zeroes contains between one and ten billion protein molecules that means that you have as many protein molecules in your body as there are stars in the known universe now each different cell type in your body makes a different kind of protein a different set of proteins like the rods and cones and my eye that are detecting light right now and the the neurons in my brain that are interpreting that light and enabling me to see you right now so then it make they make a particular set of proteins unique to it and with like any complex building project you can imagine that the process of protein synthesis needs to be tightly regulated so that the right protein is made at the right time and in the right place but of course with anything so so complicated it's perhaps not surprising that there's an occasional mistake a fault and the algorithm let's go back to that metabolic chart it's estimated that one in two thousand newborns are born without the ability to make one of the proteins on this chart that therefore they have lifelong complications due to inborn metabolic errors let's take what just one of those let's talk about vanguard fees disease or glycogen storage disease one this is due to the lack of a protein circled here and read whose job it is too to to release stored sugars so that you can maintain a healthy blood sugar level while you're fasting so vanguard disease patients can't fast they must constantly

eat small amounts of carbohydrates including getting up every one or two hours during the night to eat raw corn starch now imagine the toll that this takes on parents if they are ever to miss a feeding of their child their child could slip into severe hypoglycemia seizures and possibly death but even if these patients can keep up this endless feeding cycle they are plagued by lifelong complications including delayed puberty frequent infections kidney disease and liver cancer so is disease is just one example of a disorder where we know what protein is missing what if we could give those patients back the ability to make that missing protein then we could actually treat their disease instead of just managing their symptoms and that's where m r and a comes in that's also where i come in you see i spent the better part of my career as an academic doing curiosity based research into the fundamental principles of how proteins are made and my specialty was messenger are in a like proteins messenger are in a is our long chain like molecules composed of building blocks the for building blocks that make up messenger are in his form what is known as the genetic code as their name implies messenger are in a scary messages messages that are translated by your body in order to create proteins thus messenger are in a is our our the language of life and the human body has a lot to say so every like proteins your cells are chock full of messenger are an egg every one of your thirty trillion cells has hundreds of thousands of messenger aren't a molecules messenger are in a are an essential component of all living organisms so when you are eating protein rich foods you're not only eating protein you're also eating lots of messenger or renee your body takes the messenger are in a and the food that you consumed breaks it down into those component parts and then build new messenger are in a is specific to your needs now let's this this continual destruction and rebuilding is a feature true of almost all proteins and messenger on isn't your body let's take for example the in the circadian clock this is the timer and your body that tells you when to be active and went to sleep the proteins that make up this clock appear and disappear with remarkable regularity every day the way that this is accomplished is that your body makes the messenger are in a is that encode those proteins appear and disappear every day every day for the red for your entire life you get your daily dose of clock messenger are in a is producing clock proteins now three

properties of proper medicines are that their effects are dose dependent and that they can be given over and over again to produce the same effect. mRNA is our transient; the amount of protein produced is dependent on how much of that mRNA we have and how often we dose it. They can be induced over and over again to produce the same effect. So while it seems so simple, if we could treat a disease via mRNA, if there's a protein missing to treat disease, then we could simply give a few copies of that mRNA to the body for it to produce that protein. If that protein is only needed once, maybe a single dose would suffice. If a protein is needed multiple times, then we can dose it over and over again, and that's exactly what's happening. So when I went on clinical trials that govt this morning, it turns out that there are over one hundred and seventy-five clinical trials now open using mRNA-based medicines that are recruiting patients. Another fifty for clinical trials are waiting and the rings ready to be open. So they're this is there is a coming tsunami of mRNA medicines. Last year, Moderna and AstraZeneca reported positive results from a clinical trial where patients who during open heart surgery were dosed with messenger RNA injected directly into their heart muscles that told their heart muscles to grow new blood vessels in order to get around clogged arteries. In other clinical trials, we were repeatedly dosing patients with inborn metabolic errors to treat their metabolic disease. In fact, one of those clinical trials that's currently recruiting patients is for Fabry's disease and for cancer patients, we were creating personalized cancer vaccines. These vaccines are meant to train their bodies, their immune systems to attack their cancers. These are truly personalized medicines, one vaccine for one person. Now for personalized cancer vaccines to be the most effective, we need to get the vaccine made and back to the patient as quickly as possible. We aim for a turnaround time of forty-five days. By January of twenty twenty, we had already manufactured quality controlled and delivered to several dozen patients personalized cancer vaccines so we had the know-how and the capacity to manufacture vaccines. We were really thus when the sequence of the SARS-CoV-2 virus was posted to a public web server on January tenth, two thousand and twenty, we got immediately to work. Within two days, we had agreed with our collaborators that NIH on exactly which form of the spike protein to put in

our vaccine because we had done so many times before it then took our mRNA and a design team just one hour to design the mRNA in a way that we immediately put on to our manufacturing equipment we were then able to make that are in a get a quality controlled pharmaceutical finish and are shipped off to NIH for the clinical trial in forty five days now what I find truly remarkable is that that mRNA and a sequence that we that took us one hour to design is the same mRNA and a sequence that went into your arms that we ended up in spike facts are now fully a proven vaccine one hour design a medicine that has saved countless lives it still gives me goosebumps every time I talk about it so what does the future hold well I've already told you about regenerative medicine and personalized cancer vaccines for cancer patients we can also send and by directly injecting it messenger aren't a and their tumors we send and instructions telling the tumor cells to self destruct or having the tumor cells send out signals to the immune system to beckoning the immune system to attack for patients with autoimmune disorders we can send and signals that tamp down their overactive immune systems and we and others are rapidly making many more messenger and a vaccines because messenger on a vaccines can be produced so quickly and rapidly they're very they're really well suited for newly emerging diseases as well as other viruses like the flu that for that we do variants come out every year and the vaccines need to be updated but one of the exciting things about mRNA medicines is we're not limited to sending and the instructions for one protein and a time and already medicines can be easily multiplex therefore we're working on a combination vaccine for covered flu and respiratory syncytial virus or RSV all leading causes of hospitalization and death and the elderly and we're hoping that this will then be an annual booster that you will get just like the flu vaccine so finally the very modest footprint that of that of the manufacturing equipment for making messenger mRNA means that they can be made almost anywhere in the world and to take this to an extreme the American defense department started a program and two thousand and nineteen and we're working with them to miniaturize the entire process so that it couldn't be fit into a single shipping container for rapid deployment anywhere in the world so such a Finnish I hope I've convinced you that we have entered

an entirely new era of medicine having learned to speak the language of em are in a the language of life we can now use it to create medicines that are just for one person like a personalized cancer vaccine or can be rapidly were produced and distributed to entire populations like the coven nineteen vaccines and the best part the best part is were simply tapping into your body's own ability to make it's own medicines thank you