Sue Nelson
Hello, I'm Sue Nelson and welcome to the Create the Future podcast, brought to you by the Queen Elizabeth Prize for Engineering. Celebrating engineering visionaries and inspiring creative minds.
[Music]
Today's guest is a brilliant chemical engineer and entrepreneur, who's won so many awards, we'd reach the end of the podcast if I tried to list them all. But here's just a few; The Kyoto Prize, the Charles Stark Draper Prize, the Max Planck Research Award, and in 2015, the Queen Elizabeth Prize for Engineering. Professor Robert, or Bob Langer was born in Albany, New York, got a chemical engineering degree from Cornell University, and a Doctorate from MIT. And it was during his postdoc in the mid 1970s, that Bob developed two technologies while working on how to restrict tumour growth and on controlled release drug delivery systems. This drug delivery innovation won him the Queen Elizabeth Prize. It's led to new treatments for brain cancer as well as other diseases, and also played a role in the COVID vaccine for which we are all incredibly grateful. And if that's not enough, he's known as the founder of the field of tissue engineering. Welcome Bob, to the Create the Future podcast.

Bob Langer
Thank you so much for having me.

Sue Nelson
Now, let's start with that drug delivery system, because when examining what you've actually done, it reminded me of Doctor Who's method of interdimensional travel, the TARDIS which as sci-fi fans know may look like an old police box, but it's a lot bigger on the inside. And that's because you use small particles to deliver much bigger drug molecules. Now, is that a fair representation?

Bob Langer
It is a fair representation. The little pill that Gio Traverso and we developed at MIT and now being further developed by Novo Pharmaceuticals, Novo Nordisk. You know, basically, we came up with a way where you can actually swallow something and have it inject something in the stomach in a way that it doesn't hurt. But one of the key points is making sure that when we do the injection, the injector is always facing the stomach wall. So the thing is, when you swallow something, it's going to tumble, and we want to make sure it always tumbled in a way so that the portion where the injection takes place spaces the stomach wall. And to do so we modelled it after a leopard tortoise, because it has the exactly right weight distribution, so that it tumbles in exactly the right way.

Sue Nelson
So how do you manage that, that you get this even weight distribution? I mean, in theory that sounds quite simple.

Bob Langer
Well, it's actually not and even weight distribution, it’s an uneven weight distribution. If it was even then it wouldn't probably tumble the right way. So we actually have it weighted in certain ways. And really, we modelled it after a couple of things. I mean, the leopard tortoise is the main one, but some children have what's called “weeble wobble” toys and those are also weighted in an interesting way. So by changing the weight distribution, no matter what you do, you can do what's called self-righting. In other words, I could throw it up in the air, it would land you know, let's say you didn't swallow it, I could throw this little pillow up in the air you know quite a distance it would land on the floor, it might tumble around there too. But no matter what, it would end up with the portion we want facing, in that case the carpet. It's really because of this self-righting principle,

getting the weight distribution exactly right. So that no matter how it tumbles, it will always tumble with the part you want facing in that case the carpet and of course in the case of a person your stomach wall,

Sue Nelson
And which drugs were proving difficult to deliver from taking a pill before your innovation?

Bob Langer
Well, a lot. I mean, one of course that a lot of people were interested in, and Novo Nordisk in particular, is insulin. But I think any large molecule, including messenger RNA, and siRNA, and DNA, any proteins, any of those, antibodies, all of those are generally not delivered by mouth they're generally injected. And of course, if you have something like insulin, which a lot of little children take, they don't want to get injected. And in fact, there's a terrible compliance problem with getting people injected. And so, you know, so that's a concern. So there are really many drugs that people just don't swallow, because none will get in. Even small molecules that are destroyed by the liver would be amenable to what we're doing.

Sue Nelson
And what was it that made you realise you had a solution?

Bob Langer
We had this idea of using micro needles a long time ago, that's kind of how we started. And then, because you could swallow microneedles, we'd worked on microneedle patches for transdermal delivery, we are still working on that. But we also wondered whether you could swallow these, and then it just evolved from there. I mean, but that was kind of the first step, you know, and then later on, you know, we tried to figure things out step by step, did you need microneedles, or could you have a full needle? What should the pill look like, so to speak? How do we solve all the problems that the needle gets shot out at the right time, that it doesn't hurt, that it's reproducible, all those kinds of things.

Sue Nelson
When you started this, did you realise it had an application for very specific types of diseases immediately?

Bob Langer
Well, our thinking, and this is true for an awful lot of the things we do, is that our thought was that it could be useful for many diseases. Certainly, insulin and diabetes were one but really we kind of viewed this as a platform technology. Just like when we first developed nanoparticles for drug delivery. That we viewed, it could be useful for almost anything.

Sue Nelson
Now, one of the worst brain tumours is something called glioblastoma. What is it about this disease that makes it so dangerous and difficult to treat?

Bob Langer
Well, cancer in general is often difficult to treat here, of course, the type of tumour that it is, it spreads in a certain type of way. And it's in a place, the brain, that's hard to get to. So I mean, you have to a lot of drugs would have to go through the blood brain barrier, and usually they don't. And the tumour often spreads in a lot of places, brain surgery is certainly one way you can do it. But usually what's happened in the case of brain surgery is that, first people would certainly prefer not to do that, clearly. But secondly, you know, it often comes back. So it's been a very tough, tough disease. It still is a very tough disease.

Sue Nelson
And so your drug delivery system for treatment of brain cancer, how do you deliver what's effectively chemotherapy directly to a tumour site?

Bob Langer
This is called the Gliadel wafer. It really started with research we did in the early 80s, on creating new materials that would dissolve kind of the way a bar soap dissolves. But what we did is this sort of family called polyanhydrides, that we developed materials. And then we collaborated with Henry Brown, who's now chief of Neurosurgery at Johns Hopkins. And the idea was that Dr Brown and really any neurosurgeon operate on a patient they remove, this is brain surgery, they might operate on the patient, remove as much of the tumour as possible, but then before they close up the brain where the tumour was, and maybe still is because it may be hard to get all of it, they put these little wafers that are made of this material we designed, along with a chemotherapy drug, because you're putting it right where the tumour is, or was that that's how you do it. It's really physical placement, by the neurosurgeon that you use to do this, and over time the drug comes out, and also the material completely dissolves.

Sue Nelson
And how has that improved over the years?

Bob Langer
This particular system has been used for the last 26 years in over 30 countries. But the hope would be someday, of course that you could use better drugs right now the drug that's being used is BiCNU, which is a okay drug, but not a great drug. And really, I think the principle of local delivery, which we started, and now is being used in heart disease for drug-eluting stents and other things, you know, I think you could put better drugs and then BiCNU, the challenge of course, is that it always takes a lot of time and money anytime you know, put a new drug and a new drug delivery system. or even develop a new drug.

Sue Nelson
And would you direct delivery drug systems, are they always just one drug or can you have multiple drugs on them?

Bob Langer
You can have multiple drugs. I mean, you know, generally, of course, from an approval standpoint, from regulatory authorities it’s useful to have one drug. We've actually made drug delivery systems with as many as 10 drugs in them, you know, and shown that they work in animals. But there's probably no limit on the number that you could put in if you wanted to. We actually are working on a delivery system for hearing loss, where we actually have two drugs put into a delivery system.

Sue Nelson
Now, this is all pretty astounding stuff with we're talking about here and just sort of casually mentioned so many diseases where technology and innovation is helping. So let's go back to university, you know, coming towards the end of your chemical engineering degree. At that point did you have a clear career path in mind that, I am going to work in this area designing drug delivery systems?

Bob Langer
No, I really didn't have a very clear idea at all. In fact, when I was finishing my graduate work, you know, most of all, this was the 1970s. And almost all my friends went into the oil industry. And so I really thought I'd probably do that too. But when I would do these job interviews, I wasn't that excited about it. And so I started looking for

ways that I could use my chemical engineering background to help people more directly. I thought about, you know, doing teaching and STEM education. It wasn't called maybe that then, but I was interested in doing that, but no place would hire me to do that. So, I thought about medicine and no place would hire me to do that either. But finally, one man, Judah Folkman at Harvard Med did.

Sue Nelson
So it was when you were doing your postdoc then, at Harvard Medical School, and you were also working at Children's Hospital in Boston, I believe. It sounds like this is where the magic happened, this is where everything sort of came together?

Bob Langer
Yes. What happened is, Children's Hospital is a part of, well, it's one of the Harvard Medical School hospitals. And Dr Folkman was there and, you know, he had this idea that if you could stop blood vessels from growing, that might be a way to stop cancer, which I thought was an incredible idea. That being said, I had no background in biology, I still don't, and a lot of people didn't agree with him. So, my job was to prove that angiogenesis or blood vessel inhibitors did exist. And in so doing, isolate the first inhibitor. So I worked on that and one of the key problems in that was developing what's called a bioassay, a way to study blood vessels from in growing, and that wasn't so easy. So we had to develop these delivery systems, which would often be tiny particles that could deliver any angiogenesis inhibitor or stimulator up for a period of time. And that's where I got involved in trying to come up with ways to create microparticles and nanoparticles that could deliver large molecules.

Sue Nelson
I mean, you sort of hinted at it there, you know, just saying that, you know, you had a few doors closed for you, let's say. Have you had a lot of setbacks, earlier on in your career?

Bob Langer
I did, actually, I couldn't get a job at first, you know, I had an awful lot of rejections. You know, we published a paper on the angiogenesis inhibitors, the first angiogenesis inhibitors, and the Journal Science and 1976, and a paper on tiny delivery systems for large molecules like nucleic acids, which includes RNA and also includes, you know, also included proteins. And that was a nature in 1976. But nonetheless, when I first gave lectures on this work, they were ridiculed. People said that what I was doing was impossible. The consequence of that is my first nine research grants were rejected. And I applied to chemical engineering departments, which took for faculty positions, that's my background, but no chemical engineering department in the world would offer me a faculty position. They, I think, thought this bio stuff I was doing didn't make any sense. I finally got a job in a nutrition department. But the year after I joined that department, the faculty head of that department left. So a lot of the senior faculty in the department decided to give me advice. And their advice is I should leave too. So that was a pretty inauspicious beginning. I just though was persistent. I got lots of other rejections too. I still do.

Sue Nelson
And do you think this was because you were doing something that actually today is encouraged, which is cross disciplines?

Bob Langer
Yeah. Well, I think it is. That was certainly a part of it. I was doing across disciplines, particularly in areas that people weren't doing very much back then. And I also, you know, I don't know that I want to say that it's so encouraged today, it's certainly encouraged in some circles. But still, if you go to most universities, there's really not a lot I don't, you know, buildings that are interdisciplinary. We started one at MIT and the Koch

Institute, where I am, and Stanford and Georgia Tech and University of Chicago and, you know, definitely some other places do this kind of thing. But I still don't know that it's widely accepted by any means. I still think some people look down on it. When I started doing this work, it was very much looked down on.

Sue Nelson
And what do you think your engineering background brought to this work? Do you think it made you think differently to your colleagues who perhaps didn't have that chemical engineering background?

Bob Langer
I think it did. Let me actually give you an example, which I think will illustrate this in a pretty graphic way. So I, you know, when I went to Boston Children's Hospital, as you mentioned, I was the only engineer there, you know, and as you and I talked, you know, I began to develop materials for delivering nucleic acids and things like that, and cancer drugs. So I was very interested in materials. And I kind of was curious, how did materials find their way into medicine, you know, different materials. So what I found is almost always the driving force for bringing materials into medicine were medical doctors, and what they almost always do is go to their house, and pick some material in their house that kind of resembled the organ or tissue they wanted to fix. So for example, in 1967, some of the clinicians at National Institutes of Health in the US want to make an artificial heart. So they asked what object in their house had a good flex life like a heart, and they chose the ladies girdle, that's same material that the ladies girdle is made out of is what the artificial heart is made out of today. Because see, once you start down that path, it's very hard to change. A second example are breast implants, with some of the people who were designing them many years ago wanted was something that was kind of squishy, so they actually picked the material and a mattress stuffer. But if you think about it, that's not necessarily a great way to do things, right. The artificial heart, you know, a lot of times when blood hits the ladies girdle material it forms a clot, the patient gets a stroke, and they could die because there's the clot goes to the brain. The breast implants have also had issues. So, my feeling being a chemical engineer, one of the things you learn as a chemical engineer is chemical engineering design. So what I started doing was asking the question, “what do you really want in the material from an engineering standpoint, from a biology standpoint, from a chemistry standpoint?”, and then we would design them on the blackboard from first principles and then make them. That's actually how those polyanhydrides that are used for brain cancer are made. And that's how a number of other things we've done are developed.

Sue Nelson
That is astonishing. I did not know that. I'm just astonished that they hadn't tried that sooner. But then that's what they needed, obviously was an engineer to come in and state that. You're also regarded as the founder of tissue engineering. Did you take the same approach to that area as well then?

Bob Langer
Well that was related. Of course, one of the great things about working with medical doctors is they talk to you about all kinds of medical problems. The way that started was my colleague and friend Jay Vacanti.. I worked with him on the angiogenesis problem in the 70s. And in the early 80s he began as the head of the liver transplant programme at Boston Children's Hospital, and so he would see little babies that he would have to operate on to give them a new liver. So one day he started talking to me about, could he and I come up with a new way to create tissues and organs again from scratch. You know, so we talked about that a lot. And he, of course, had a lot of vision, he wants to ask me, could we make what I’ll call a scaffold that you could put cells on, that wouldn't have a high enough surface area to volume ratio that a lot of cells could be put on. And so he and I began talking about that. Here one day, Jay actually, you know, we originally tried two dimensional things like coins almost, but you know, they're made of materials in this case, but we couldn't get enough surface area. One day, Jay saw seaweed when he was in Cape Cod, he said, “well, could I design a material that looked like

that? And so we did, I did. And we put cells on it. And we use that to try to make artificial livers and other, you know, other scaffolds, later it would lead to making artificial skin, and so forth. But it also, again, involved a number of engineering principles in this case.

Sue Nelson
Quite early on you became an entrepreneur as well, what was the first company that you set up?

Bob Langer
Well, the first one was a little company called Enzatech, later it merged to become what's now called Alchemiz. And that was with Alex C. who was one of my colleagues and a number of my students who had worked on this. And actually, there was a food part of it, which made some of the first fat substitutes and drug delivery part, which is now you know, is part of Alchemiz, and that would help lead to new treatments for schizophrenia, opioid addiction, diabetes and other diseases.

Sue Nelson
And you've co-founded more than 40 biotechnology companies now. I mean, I hesitate to use that number because I just feel as though it might have gone up just a little.

Bob Langer
It might be up a little might be up a little but yes, you're not far off. Definitely we maybe do like one a year, sometimes two.

Sue Nelson
Wow.

Bob Langer
That's pretty good.

Sue Nelson
And that includes Moderna, a sort of name that few people perhaps were aware of until the pandemic arrived, and all of a sudden, we realise that one of our vaccines is made by Moderna. So how did that connection come about with you, is this as a result of this drug delivery system?

Bob Langer
Yes, well, in 2010 four of us, Derrick Rossi, Noubar Afeyan and Ken Chien and myself, you know, started the company with the idea of creating messenger RNA therapeutics, but one of the keys that would certainly turn out to be important is having, you know, a way to deliver the messenger RNA, you know, in this case, through nanoparticles seem to be the best way for certainly most of it, you know, and of course, we'd actually developed the first systems, that's what I mentioned, was published in Nature, to deliver nucleic acids to tiny particles. You know, 1976 we published it, like I said, people were very sceptical, but over the years, we and others would break down those barriers and design, you know, better and better nanoparticles and Moderna as well as others continued to design better and better nanoparticles, so nanoparticle are really one of the keys to creating messenger RNA vaccines, whether it's the Moderna one or the BioNTech Pfizer one both use nanoparticles, though are different nanoparticles. But that's exactly right. That was one of the key things, still was one of the key things for what Moderna is doing.

Sue Nelson

And you know, you've had an amazing career, your career still seems at its peak, and it seems to have been at its peak for a very long time. So what sort of started you off, what did what sparked that interest?

Bob Langer
I'd like to tell you I had it well thought out, I'll tell you two quick things. You know, one is when I was a little boy, you know, there were these Gilbert sets, or Rector sets, and chemistry sets and microscope sets. And I did like those, I'd get those for presents. And I always enjoyed those. And I love, you know, I set up a little lab in our house chemistry, more to do magic tricks and things like that. But really, what happened was when I was in high school, you know, I was good in math and science, I was not very good in French and English and other classes. So my dad, and my guidance counsellor said, "well, if you're good at math and science, you should be an engineer". I really didn't know that much what an engineer did, but I that's, you know, I sort of did what they suggested. I went to Cornell as an undergrad and then MIT for graduate work.

Sue Nelson
Well, that's good advice there. And, and it also sounds as though you've really benefited from key figures effectively, mentors throughout your career. What would your advice be to budding engineers?

Bob Langer
Well, I think engineering is a great profession. I mean, I think it helps you think, not only the things you learn directly, but the things you learn indirectly, you know, about problem solving, and really trying to make an impact, which I think is good. So, I think it's a great profession. I still think when somebody's a young engineer, you know, like, say an undergraduate, you want to learn fundamentals, you want to learn, whether it's biology, or chemistry or physics, you want to learn fundamentals of whatever it is. I think, later on as you become if you do decide to go into research, and you go to graduate school, or do postdoctoral work, I think there you can get more specialised, I think it's very worthwhile to dream big dreams and think about projects where, you know, that can make a big difference on the world. But I think the engineering profession is a terrific profession.

Sue Nelson
And I mentioned at the start of the podcast, you know, just some of the huge number of awards that you've received during your career. What did being awarded the Queen Elizabeth Prize mean to you?

Bob Langer
That meant a great deal to me. I mean, it was a second time it was given. The first time it was given for like the internet and the World Wide Web, you know, so I was honoured that they picked me and actually just me to receive that award. You know, actually, in a way, I have to give the award committee, not because they gave it to me, but a lot of credit, because they picked, you know, the work we have done on drug delivery for macromolecules, as being important. And then, of course, as you pointed out, just a few years later, it would become even more important, because, you know, that helped enable the COVID vaccines. But I think shining a light on bioengineering and shining a light on drug delivery systems, which, you know, an award like that does, I was, I thought that was really important because it shines a light on it and shows the world that, you know, an outstanding group of judges thought it was important.

Sue Nelson
And so did that prize, then have an impact and effectively add to the legacy to the work that you were doing?

Bob Langer
Yeah, it's hard for me to think of me as having a legacy. But I, I think, certainly to the extent that I do, sure. I mean, I think it's such an important prize, partly because of the awards committee and their backgrounds, you

know, presidents of universities, and, you know, Nobel Prize winners, and also partly because of the other people that have gotten that award.

Sue Nelson
And in fact the most recent prize went to the innovation involving permanent magnets. Have you ever used permanent magnets within your field?

Bob Langer
Yeah, we've developed what I'll call magnetically triggered drug delivery systems. I mean, it's early-stage basic work. But yes, we can use, we actually published a number of papers in the 70s and 80s, on magnetic delivery systems that you could also get drug release from. So yes, absolutely.

Sue Nelson
The year that you got the award, it was presented to you by the Queen, what was that moment like for you, as someone who's started off with so many, like you say so many setbacks, and having grants refunded, to suddenly being at that position where you're in front of the Queen?

Bob Langer
Well, it's a tremendous honour for me, I mean, the Queen was there, and you know, six members of the royal family and, you know, and they spent quite a bit of time with me and others there. My family was there, including my children, wife and sister. You know, to me, it was a tremendous honour. I mean, you know, to be there with her and her husband and be in Buckingham Palace, which is such an amazing place, I will never forget it.

Sue Nelson
It's great. And you probably know that the trophy is designed through a competition that encourages people who are interested in engineering and design, that STEAM combination. You know, you hear of actors who've got their Oscars, and they keep them in their loos. Where do you keep all your trophies?

Bob Langer
In the living room my wife has a bunch of trophies up, actually she has different things in different rooms. But there's one that's got a lot of very good awards and her big awards, like the National Medal of Science in the US National Medal of Technology, the Priestley Award, and certainly the Queen Elizabeth trophy is front and centre and, you know, they're all you know, it's certainly a great honour to me. And then my MIT office, my secretaries have various plaques up on the wall.

Sue Nelson
It must be a pretty crowded wall. So what's next for you, you know, you've already made a tremendous impact. Where are the rooms for improvement, or what areas do you see "oh, I really want to go in that direction"?

Bob Langer
Well, there's a number of we're right now in our lab, we're working a lot sponsored by the Gates Foundation to develop new medicines and new vaccines for the developing world, you know, ways that you could give a single injection, for example, for a vaccine, but have it be self-boosting, you know, where one injection would actually lead to the equivalent of maybe 12 injections, but it's, by making little nano or micro particles that might burst at different times. We're also working on better ways of giving micronutrients, again, because of the starvation issues in the developing world. And a new kinds of pills that you could swallow, but they'd last for an entire course of treatment and you take them orally, so pills that could last for a week or a month. And these would be

useful not only in the developing world, but also everywhere. And then we're also, as we talked about, working on tissue engineering, working on creating new tissues, like, you know, maybe an artificial pancreas. And we're working on things like creating, you know, brains on a chip at MIT and gastrointestinal tract on a chip with Gio Traverso at MIT and these, you know, could someday use animals a lot less for testing. And hopefully humans a lot less for testing and might accelerate drug development as well. These are all our hopes.

Sue Nelson
This just sounds incredible that there is so much more exciting work to continue with.

Bob Langer
I believe that's the case, research, whether it's with us all over the world. You know, I think it's an exciting and certainly very important time as we could see from the COVID issues, but I think it was important before, maybe even more important now.

Sue Nelson
And how do you see the future of engineering?

Bob Langer
Well, I think engineering will only grow and do better. And, you know, like I said, there's so many challenges that we have across the board, you know, I mean, I focus more on chemistry and medicine, but the others are focusing on electrical issues and computer issues, artificial intelligence. There's just so many things that engineering has and will continue to play a major role in.

Sue Nelson
Bob Langer, thank you so much for joining me on the Create the Future podcast.

Bob Langer
Well, thank you. It's an honour for me, I appreciate it.

Sue Nelson
Find out more about the Queen Elizabeth Prize for Engineering by following @qeprize on Twitter and Instagram, or visit qeprize.org. Thanks for listening and see you again next time.