UYANGA TSEDEV: So hi, girls. My name is Uyanga. And I am currently at the MIT Koch Institute, which is a building just for cancer research. And today, I'm going to talk about the biological engineering that we do in order to find and image deeply embedded and difficult-to-reach tumors.

So currently in the clinic, the number one therapy method for cancer is-- thank you-- for cancer is surgical debulking, which is basically removing of the tumor masses, and then chemotherapy. And so it's very important for surgeons to be able to locate precisely and early on in the stage of the tumor the masses that they want to remove in order to do the most effective therapy.

And so cancer cells are basically cells that have unusual dividing abilities. So they proliferate without stop. And they are differentiated from the regular cells around them by certain markers on the surface of the cell.

And so what we want to do is use these markers on the surface in the cell in order to find and then locate where the tumors are, and tell the surgeons, this is the place where you should remove the biological tissue. And you don't want to damage the healthy tissue around it. So you want to be very precise.

So there are two tools that we use in our lab in order to find the tumors in the body. The first is the custom-built imager that we're working on with collaboration at the Lincoln Labs, and the second is the biological probe. It's a little shuttle that we use in order to go ahead and find the cells in the body. So we can talk about both of them today.

So the biological marker that we use is called the M13 bacteriophage. And bacteriophage really just means bacteria eater. So it's a virus. So as with typical viruses, it infects bacteria, [INAUDIBLE] takes over the local mechanism of the bacteria, and begins to replicate itself.

So what we can do is hack this system in order to use this molecule for our own benefits. It's a very beautiful, very simple sort of molecule. It's just a piece of DNA-- so a DNA that codes for its genetic information-- and a bunch of proteins that's wrapped around the body.

And so because we can manipulate the DNA, we can change the peptides that are on the body of the phage. And so we can change the protein so that they have specific binding abilities to certain materials or certain ligands, or certain markers. So this is the tumor cell

markers that I'm talking about.

We can change the protein at the head of the virus in order to bind specifically to the surface of a cancer cell. And we can change the proteins on the body of the virus to bind to a specific imaging agent or therapy agent that we can then shuttle to the surface of our cells.

So for our system here, the imaging agent that we chose is called a carbon nanotube. And so a carbon nanotube is just a piece of graphene that's been rolled up. And what graphene is is it's just a single layer of graphite. And graphite is what you find in your pencils, in lead.

And so it has very interesting optical and electrical properties, and it's very well-studied. But for us, what's interesting about it is the wavelength at which it emits light. This is in the second window near infrared wavelength.

And so it's slightly longer than the visible wavelength. And the cool thing about this is it's able to penetrate deeper into the biological tissue. And you have less scattering and less interference from the surrounding materials.

So finally, this is the design of our shuttles that we send in to find tumor cells. We have the M13 bacteriophage, which has a particular protein at the head that detects the tumor cells. And we have on the body the CNT, the carbon nanotube, that is going to light up and tell us this is where we should go ahead and remove the mass.

So the first model that we have actually done in our lab is on ovarian tumor. And ovarian tumor is one of the tumor [INAUDIBLE] that is very difficult to detect early on. Unlike things like breast tumor, you can't feel it. And usually when the surgeon or the doctor diagnoses, it's quite late in the stage of the tumor.

So it could have turned metastatic. And metastatic means that the tumor cells have detached from the body and traveled to other parts of the body, and so proliferated other tumors throughout the body. So this is a stage you don't want to reach.

So it'd be very cool if you can put our probes into mice with a ovarian tumor, light up the tumors, give the surgeon the image, and the surgeon can go ahead and remove the tumors, and the mice will then survive. So this is a first step in putting our system to its clinical application.

So this is what happens in real life. You see here the stomach cavity of the mice. And in the

bright orange, you see all the tumor masses that have lit up. So we have injected the mice with trillions of our tiny little molecular shuttles that carry our CNT to the location of the tumor.

And using our imager, which we have built with help from the Lincoln Labs, the surgeon is able to go in and remove all these nodules. And the cool thing about the nodules here is we're getting the ones that are even below a millimeter in diameter. So usually, when a surgeon goes in without any guidance, he might miss these because he's just going by eye. But because he has the imager, he can go ahead and remove most of the tumors.

So here's an example of what we're doing in real time. So during surgery, if the surgeon can directly refer to the images that he's getting, then he can go ahead and implement our technology in a very real way. So here, we see Dr. [INAUDIBLE] from MGH. He's doing surgery on mice.

And you can see on the screen, he can see brightly lit up-- this is where the tumors are, and this is where I should take it out. And so here's a serial image of what's happening. So here's the probes lighting up where the tumors are.

This is what happens when the surgeon goes in by eye and is like, OK, from my experience, this is where I should take out the tumors. And you see that there's quite a bit of mass left. But if we have the imager, then we have a much cleaner image at the end of the surgery. And so there's a lot less of a chance that the tumor is going to recur.

So for me personally, there are two things I'm doing in order to expand on our system that we have already built. The first is manipulating the M13 phage to different geometries. So I call this inhophage. Inho just means small in Portuguese.

And so based on the aspect ratio, which basically is the diameter versus the length of our phage, they might have very different traveling abilities in the bloodstream. So because of their oblong shape, they have a tendency to stick to the walls and tumble around. But if we can change this shape to an optimal size, then there's a chance that they will travel for a longer period of time in the bloodstream, and so find the tumors that are farther from the site of injection.

The second thing is we are expanding on the library of cancers that we can attack. So so far, we have looked at ovarian tumor, and now we want to look at brain tumor. And the most difficult thing about brain tumor is the blood-brain barrier.

So it's just a layer of cells that separate your blood from the matter in your brain. And the molecules that pass through are very specific and very small. So it's very hard to deliver from your bloodstream various drugs or imaging agents to the actual brain mass.

So what we have done here is actually engineer the head peptides-- so the proteins at the head of our phage-- so that it allows for travel across the blood-brain barrier so it can deliver these imaging molecules to tumors in the brain.

So one thing to remember here is that the scale at which we're working is very, very small. So if you look at CNT or our phage, really, it's about 100,000 times smaller than a strand of your hair. So these are really, really tiny things.

So when I make these small phage, they're even smaller than our regular phage. Our regular phage is about 800 nanometers. So here's an example of 280 nanometer phage, 100 nanometer phage, and 50 nanometer phage.

So when I make them and I want to look at them, it's really hard because they're so small. And you can't just use regular light microscopy to detect them.

So another interesting thing that I do is use atomic force microscopy. I don't know if you've heard of it. But what it is is basically you take a sample, and you have this very, very tiny needle that scans across the surface. And so you're getting a topology of the surface.

And from that scanning, kind of like reading Braille, you get a good idea of what the profile of your image is. So these are the images that I get from this sort of needle probing.

For the brain tumor, another interesting factor-- not only can we bring the phage to the surface of the tumor-- so this is tumor here shown in green. This is tumor that actually has green fluorescent proteins, so that means they glow. And if we send in our phage, we see that, oh, yeah, our phage goes ahead and coats in red the tumor.

But then the other thing we notice is that the phage is actually internalized into the tumor cells. So the phage comes and attaches to the surface, and then the tumor cells eats the phage.

So in the blue here is the nucleus of a phage. And in the red spread around the nucleus in the Golgi region is our phage. So it just tells us we can possibly deliver things to inside the cells of the cancer.

So that means we could send in therapies that disrupt the function, and so in this way, kill the tumor cells. And so can we not only detect where they are and see if it can remove them effectively, but we can also locally cure them.

So overall, today, we've looked at the very real medical impact that we can do with imaging and the probe that we have biologically engineered in our lab. And the two things that I've done is look at what we can do to change the geometry, and what we can do to change the different cancers that we can attack.

And all of this work, of course, is impossible without the collaboration that happens between the colleagues I have at the MIT Koch Institute, as well as the scientists we have at the Lincoln Labs. And so that's another really cool thing about this project. It's so very broad, and so it brings in so many different techniques and brings in so many different people. And so I really want to thank them.

And another aspect of this work that I really find meaningful is that I am personally funded by families that are affected by these types of tumors, these types of diseases. And so I really want to thank the Goodwin, [INAUDIBLE], [INAUDIBLE] and [INAUDIBLE] families who have been really generous with their funding for this project.

And finally, I want to say that for me, the M13 is kind of a building block. We're here all as Girls Who Build. And so for me, for my building project, it's the M13. And I hope that you guys are able to understand from this that as an engineer, for me, it's really just about finding creative ways to use my building blocks to make a difference, to address the problems that I think are most important to me.

And so thank you very much for listening. Please feel free to ask me any questions. I can talk more about myself, or I can talk more about research. But yes, thank you.

[APPLAUSE]

PROFESSOR: Any questions for her?

UYANGA TSEDEV: Yes?

AUDIENCE: You were using specific examples for the cancer, but can these detect any type of cancer, or is it just specific, or a couple of types?

UYANGA TSEDEV: It can detect any type of cancer as long as you have a specific differentiating marker on the cancer that you know of. So not only is this useful in cancer, it's also useful in detecting any other material. As long as you're able to modify the head so that it is specific to that material or to that cell, then you can do that, which makes it a very elegant, very cool molecule, which is why I think it's something I should be using.

[CHUCKLING]

PROFESSOR: Any other questions? Great. Thank you, Uyanga.

[APPLAUSE]

UYANGA TSEDEV: Thank you.

[APPLAUSE]