Harvard Medical Labcast
February 2016

Genetics in Space
Improving human health on and off the Earth's surface

Ting Wu
Interviewers: Stephanie Dutchen, Jake Miller

STEPHANIE DUTCHEN: Hello, and welcome to the February 2016 Harvard Medical Labcast. This podcast is brought to you by Harvard Medical School's Office of Communications in Boston. I'm Stephanie Dutchen. Our regular co-host, David Cameron, has left us for a new job at Harvard. So I have roped my colleague Jake Miller into co-hosting instead. Thanks, Jake.

JAKE MILLER: You're welcome.

DUTCHEN: We miss David, but we do have a terrific topic for today's conversation. HMS Professor Ting Wu spoke with me about genetics research and space travel.

MILLER: You know, Joni Mitchell and Neil deGrasse Tyson like to say they we're made of stardust, but it's a long way from being made of elements that were furnaced inside of stars to packing up and leaving earth.

DUTCHEN: True. And I, perhaps like you and like them, am such a geek about space travel, now and in the imagined future. So you will have to forgive my enthusiasm during the conversation. But it turns out that many scientists are excited, too, about exploring how genetics can improve human life beyond Earth. HMS just this month launched a consortium for space genetics that you can learn about on our website.

And Ting talks about work going on in her lab, in the genetics department and across the country, on topics ranging from protection against cosmic radiation damage, to how people can stay physically and mentally healthy on trips that might last 20 years or even multiple generations.

MILLER: Far out, man. That's one cosmic trip.

DUTCHEN: All right. Let's go to the interview.

[MUSIC PLAYS]

DUTCHEN: Thank you for coming to talk with us today.

TING WU: It's my pleasure.

DUTCHEN: So you actually are the one who suggested this topic. And I would love to know why. What attracted you to thinking about genetics as it applies to space and space travel?

WU: I think, like many people, I've always been interested in space. I remember when my father took me to the ocean, and I could see the curvature of the Earth. I suddenly felt a little claustrophobic. I could see that the Earth was small.

But more recently, I think what brought me to this topic very seriously is that there are astronauts who go into space and come back with serious health issues. Or they have serious health issues in space. We are at a medical school, and our job is to address ailments for the human species, regardless of how they became ill. And so we need to take care of our astronauts. There have been over 500 people who have spent a significant amount of time in space. And we need to start thinking about that issue.

The other piece is that, as you know, I run the Personal Genetics Education Project. And we spend a lot of time thinking about where personal genetics is going and whether our communities are prepared for the decisions that they will need to make, the choices that they'll have for their life and their work and their play. And one interesting intersection is the application of genetics, genetic technology, genetic information, for living, working and playing in space.

DUTCHEN: So where does genetics intersect with space travel, now or in the science-fiction theoretical future?

WU: Space, we'll start with now.

DUTCHEN: OK.

WU: Then we can get to the science fiction later.

So I think the intersection is just beginning. Well, actually, of course, it's 100 percent intersected, because when human beings go into space, they bring their genomes with them. And the way they behave, the way they respond to the stresses of space, depends a lot on their genome.

I think, as with any job on Earth, the hope is that information about a person's genetics can help enhance their ability to do their job, enjoy their job and enjoy their life. So part of it is using the genetics to help prepare an astronaut to know how they're going to respond to the stresses in space and to best prepare themselves when they come back from space to recover as efficiently and effectively as possible.

For example, it's well known that long-term stays in space lead to bone loss. Many astronauts suffer ocular problems. And there is no way currently that an astronaut can avoid the increase in cosmic radiation and therefore damage to their body, especially their genome. So understanding what the genetic capacity of an individual is to, for example, repair damaged chromosomes will help that astronaut understand what vulnerabilities he or she may have.

DUTCHEN: So when you shoot somebody up in a spaceship, they don't have the protection of Earth's atmosphere anymore, right? So they're much more exposed to this bombardment of cosmic radiation, and that can't be good for their DNA. If I remember correctly, that's something that you're studying here in your lab.

WU: Yes. So actually, many labs study the process of DNA damage and DNA repair. In fact, beautiful studies have revealed the pathway of genes that get turned on. And some of them get turned off. These genes make products that detect damage and then enable that damage to be repaired, hopefully perfectly, but sometimes a little imperfectly. The better we can change that balance towards the perfect, the better we are. And that is why much work has been done to try and understand the DNA damage repair pathway.

My lab has a slightly different take, and we came to it somewhat… oddly. My lab studies very basic properties of chromosomes; in particular, how chromosomes are placed inside the nucleus. We believe that the placement of chromosomes and the way they're folded will one day be as strongly considered heritable material as we now think of DNA and epigenetic marks.

So in the process of studying that, we were made aware of a very strange set of sequences called ultraconserved elements. And what I'm going to tell you now is really speculative. We like this model. We are studying it, fully aware that we may be wrong. But it's been great fun. And the model, while it could well be wrong, helps us to frame our experiments.

DUTCHEN: OK. Disclaimer noted.

WU: Thank you. Our model is that these very strange sequences, which seem to have resisted change for 3 million [or] 5 million years -- that's well before the dinosaurs. It's before reptiles, birds and mammals diverged from each other.

DUTCHEN: Long time ago.

WU: So these are a long, long time ago. These sequences have not changed. And we really -- the field -- by "we," I mean the field -- has no well-accepted, proven explanation for their ability to withstand all those years. While their brother and sister sequences have been mutated and changed, they have not. Through a set of arguments I won't go into now, we think that these sequences do a very special thing. Basically, their job is not to change.

And in order not to change, they manage to maintain the integrity of the genome that's around them. And when they see too much damage going on, they actually send up red flags and cause that cell to be culled from the body.

So the simple connection to space is this. If we can understand how these sequences work, maybe we could induce them to be even better in astronauts. So astronauts can go into space. Their DNA can get damaged. We know it gets damaged much more in space than here on Earth. But when it's damaged badly, those cells are simply culled from their body and are not allowed to develop into tumors, which is one of the outcomes we think happens when a genome is damaged badly.

DUTCHEN: Interesting. So thinking, again, about the different ways that the study of genetics can be applied to people going into space: A couple of years ago, you co-hosted a seminar that was held here at HMS, where you had people from the Department of Genetics and then people from Jet Propulsion Lab, people from all over the country, who came and just shared their thoughts, speculative or based in the near future or current research, on all of the different ways that the study of genetics could improve the lives of astronauts and help humanity get off the planet that birthed them, now or in the distant future, when we have somehow destroyed our planet beyond being able to live on it, which was great fun.

I was able to go. And I know you talked a little bit about the ultraconserved elements there. But there was a lot being discussed about all the different ways that space travel can impact the human body and what we might be able to do to improve that experience. I mean, what was that like for you to be part of?

WU: It was great fun. I will say, in all my years as a research scientist, I have never seen the instantaneous excitement over a speaker or a symposium as I saw for that particular event. I think that was one of the most rewarding parts of the symposium. Now, Adam Steltzner came and told a beautiful story about putting Curiosity on Mars, a very inspiring story. And then we had Dorit Donoviel come from the National Space Biomedical Research Institute. She summarized a lot of the research that she oversees, having to do with many physiological parts of our body. And then we had a number of faculty from the Department of Genetics.

I'd like to point out an interesting piece that Susan Dymecki mentioned, which is the concern about how human beings can survive in terms of their behavior, whether they're happy or not in space, the stress on a person's sense of wellbeing. There are many who believe that, in spite of all of the physical stresses on human beings that makes travel in space difficult, it's actually the stresses on an astronaut's mind that people are most concerned about.

And she mentioned how in some contexts, chess is banned.

DUTCHEN: Chess is banned--

WU: Chess is banned--

DUTCHEN: --in space?

WU: --in space, because in a small, confined space, the stress of chess can be a little too difficult.

DUTCHEN: My goodness.

WU: Yeah. So Susan talked a lot about her studies of understanding how the brain is wired, what parts of the brain control breathing rate or emotions. So that is a very important part of space genetics that people often don't think of as something that needs to be addressed.

DUTCHEN: I would say that would be unexpected, yes.

WU: I've talked with people from NASA, and they generally agree. That is a piece that has to be solved. And these long trips, they're talking about trips that will take ten or more years going one way, with just a small group of people. And after a while, you can imagine that's one that's going to weigh most heavily.

DUTCHEN: That's right.

WU: And then we also had people -- Bruce Yankner talked about the impact on cognition. People in space need to be on the mark all the time, stay on their toes. What happens to an aging brain, an aging brain under space? Can we understand what molecules with genes protect the brain, what genes don't?

And Gary Ruvkun talked about trying to understand if life has already arrived on certain planets, Mars, for example, before we get there. It helps us understand where we come from, where we're going, how much we want to protect a planet when we arrive there.

George Church talked about what some people have come to call protective variance. So these are variations in the genome that, for example, can increase your bone density. Might that be useful in counteracting bone loss? We'll have to see.

There are variants that can reduce pain sensation. Will that be useful in cases where you might have to do, for example, surgery in space? We talked about the microbiome, the issues of whether we want to bring our microbiome into space or leave it behind. I know that in the microbiome world, people are wondering how much the microbiome affects one's day-to-day sense of wellbeing. Will that help?

DUTCHEN: So there can be some variants that astronauts have that are beneficial to the special types of stresses that you would experience during space travel, long- or short-term. I can imagine a future in which that sparks all kinds of debates about who gets selected for those kinds of programs. Do you choose people to become astronauts who have those variants, or do you somehow engineer those variants to whomever is chosen to go? And obviously, we don't have answers for any of that, but I can imagine that would fire people up.

WU: Yes, and those are very good questions that I think are on the table. People recognize very much all the potential benefits of genetics. And they really want to maximize the benefits, bringing in, as little as possible, confounding negative aspects of genetic information. I think this is one of the topics that is going to engage people. And thank goodness if it does, because we need many, many different kinds of input to understand how we're going to answer those questions.

DUTCHEN: So, OK, you promised we could get to the science fiction stuff. One of the last speakers at that symposium was David Sinclair. And he was spinning out all these fun speculations about if we're going to go on these multigenerational space trips to, I don't know, other solar systems, other galaxies, that maybe there would be ways that we could tweak the human genome so that people would live longer.

WU: Yes.

DUTCHEN: Or that we could somehow engineer the babies that are born in space to be more adapted to that environment. I mean, it was super fun to think about. Is that something that you think about, too?

WU: So yes, I think about it from all different points of view. These trips are very long. How are you going to get to some of those planets that are so far away? We're talking about generations of humans. And one strategy is to figure out how a person can take off from Earth and live the entire set of years and arrive at the other end fully functional and able to do the task.

Another strategy is to figure out a way where that person can have progeny with other people and train them, knowing that those progeny will want to do that at the other end. That's a tall order. Another thing we think about is the science fiction-like possibility of holding a person in the developed state, trained and ready, holding them so they do not change and do not age, and end up generations later ready to go.

DUTCHEN: Like in one of those icy cryopods?

WU: Exactly. And then there's [a question of] how you hold them. Do you hold them in their current state? Do you freeze them? Do you dry them down? Do you print them? These are all things that are on the table to think about.

I can tell you there are no technologies now that make anyone confident that any of these will work. But the past 100 years of genetic research has shown us that we can do some pretty amazing things.

DUTCHEN: And you have a postdoc coming to your lab, this summer is it?

WU: This spring.

DUTCHEN: It's going to be this spring, very soon. He's going to be working exclusively on a project related to space. Tell me more.

WU: So my laboratory, as I mentioned earlier, is very interested in how the genome is arranged and packaged in the nucleus. It's been a long project. We've been building to this point over several years. And the first step was to try and develop a technology that would allow us to see the genome at the resolution we would need to see it at, in order to understand folding.

So one question we have is, when you take away gravity, how is it going to affect that kind of packaging? Now, we really don't know.

DUTCHEN: It might do nothing, or it might turn everything haywire?

WU: It might do nothing. It may be that the genome has no such sense of gravity. Or it may cause some changes, which may have absolutely no effect on how the genome behaves. Or it may have some changes that will, over time, have a degrading effect on the way the genome behaves.

If it's the third one, then we need to start to think very seriously about how to counteract those results or to generate spaceships that will be able to recreate gravity for our astronauts for very, very long-term travel. You mentioned David Sinclair's discussion at that symposium about having children in space. Development is a very delicate time. It may be that adults can go into space, and these changes to their genome really won't matter too much. But development is based on thousands, millions, of very precise decisions. And so we would need to know in, for example, mice, as they develop, what happens to the chromatin structure or the structure of the genome.

And so what Hoy is going to do, my postdoc who's coming in the spring, is to -- we're collaborating with some individuals who will be able to get us cells from space. And we're going to look at, compare the genome structure of cells from space and cells on Earth, to see if we can see a difference.

DUTCHEN: I was going to ask how you study something like that. Do you just do your experiments up on a spacecraft? Or do you get to put them in one of those planes that just drops the gravity out from under you?

WU: So we've formed a collaboration with Bruce Hammer at the University of Minnesota. He grows cells, I believe, in the International Space Station and will be able to provide those to us. He also has developed a machine that tries to simulate or simulates microgravity. And we'll be able to get cells from that machine, too.

DUTCHEN: That just sounds like fun. All of this stuff sounds like fun. Is it fun to work on this? Is it fun to think about?

WU: It's great fun. It's fun to think about. It's fun to talk about. I think that scientists love getting out of their comfort zone, going to places where they're not sure they're going to succeed or fail. There's great excitement there.

DUTCHEN: Going where no geneticist has gone before.

WU: Exactly. And then seeing what we can see. This is one of these situations where we can just collect data and learn something entirely new, without having to go out and prove something. Of course, we would love to be able to prove that it's safe to spend a long time in space. Whether or not that turns out to be the case, I don't know. But it's important to find out.

DUTCHEN: Do you have an ultimate hope for what your projects or your postdoc's project or your colleagues' projects might ultimately lead to?

WU: I would love it if we could make our astronauts safer. It would be great if what we find enables us to go further in space and learn things that we can't even dream of right now. And I'm truly hoping that what we learn, for example, about these ultraconserved elements will be able to help general health issues on Earth.

We think that cancer is one of those diseases that have escaped the ultraconserved element surveillance system. And so if we can hone that system or up that system in individuals that have cancer, maybe we can literally just cull those cancer cells right out of a person's body.

DUTCHEN: That's a much more compassionate answer than maybe saying that you want them to name the first terraformed settlement after you, or something.

WU: I would give that up in a moment if we could address these diseases.

DUTCHEN: I guess that's a great note to end on.

WU: Thank you for your interest.

DUTCHEN: Oh, thank you for sharing all of these, definite food for thought.

[BELL RINGING]

DUTCHEN: And now, for this month's abstract.

MILLER: Birth control pills or oral contraceptives are more than 99 percent effective with diligent use. Still, some women do become pregnant while taking these pills or soon after stopping them. That means their unborn children may be exposed to the hormones in the pills. And very little is known about whether that causes any health consequences.

A new study from researchers at Harvard Medical School and the Harvard T.H. Chan School of Public Health offer some good news. They found that taking oral contraceptives just before or during pregnancy does not increase the risk of birth defects.

Working with colleagues in Denmark, the team analyzed data from multiple Danish health registries between 1997 and 2011. The registries included information about 900,000 live-born infants and the health of each child one year later. The researchers estimated oral contraceptive use based on the mother's last prescription fill date.

About 1/5 of the women in the study had never used oral contraceptives before becoming pregnant. More than 2/3 had stopped using oral contraceptives at least three months before becoming pregnant. Eight percent had stopped within three months of becoming pregnant. And 1 percent had used oral contraceptives after becoming pregnant.

The researchers found that the prevalence of major birth defects -- about 25 for every 1,000 live births -- was equal across all the women, regardless of whether they were on the pill. The numbers remained consistent even when the researchers factored in pregnancies that ended as stillbirths or induced abortions.

The first author of the study, Brittany Charlton, says the results should reassure women and their health care providers.

[MUSIC PLAYING]

DUTCHEN: This podcast is a production of Harvard Medical School's Office of Communications. Thank you for listening. And thanks to our producer, Rick Groleau. To learn more about the research discussed in this podcast or to let us know what you think, visit HMS.harvard.edu/podcasts. You can also follow us on Twitter, where our handle is @HarvardMed, or like us on Facebook.

Now, we leave you with an outtake from our interview involving an imaging technique called fluorescent in situ hybridization, or FISH for short.

WU: So the first step was to develop a new kind of probe that would allow us to visualize the single-copy parts of the genome. And Brian Beliveau spearheaded that project, led to the development of a new kind of FISH probe, which we call oligoPAINTS.

DUTCHEN: FISH.

WU: FISH. That's right. Fish in space. And--

[LAUGHTER]

WU: Shall I start that again?

DUTCHEN: I don't know. It was perfect.

[LAUGHTER]

WU: Oh, OK. let me do that again. I don't know why I said fish. OK. There are a lot of jokes about fish. We talk about dead fish, live fish experiments. OK.

END OF INTERVIEW