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0:00:05.7 Sarah Crespi: This is the Science Podcast for May 20th, 2022. I'm Sarah Crespi. Each week we talk about the most interesting news and research from Science, and the sister journals. First up staff news writer, Daniel Clery. We talk about the first image of the giant black hole at the center of the Milky Way, it looks a lot like a bright flurry donut, and a lot like the first image taken of a black hole at the center of a different galaxy a few years ago. We talk about why it's a good thing that they look the same. After that, we have researcher, Jason Brock. We discuss how Bottlenose dolphins recognize each other through signature whistles and a signature tastes, and what using taste and sound for identification tells us about the way dolphins minds work. And in a sponsored segment from our Custom Publishing office, Director of Custom Publishing, Sean Sanders talks with surgeon and philanthropist Gary Michelson about the need to solidify funding for immunology to support its applications in addressing infectious diseases and cancer.

0:01:14.0 SC: It's been a few years since the first image of a black hole was published. The super-massive black hole at the center of the M-87 galaxy came out around 2019, and now we have a similar image of the black hole at the center of our very own galaxy, at the center of the Milky Way. Daniel Clery is a staff writer for Science, and he's here to tell us about this image, where it came from, and why it looks so much like the first one we saw. Hi Dan.

0:01:42.7 Daniel Clery: Hi.

0:01:43.4 SC: Okay, so yeah, these look a lot of like, why don't you just briefly describe what these black hole "images" look like?

0:01:49.8 DC: Yeah, well, very, very much like the first one, it's a bright ring with a black center against a black background, but it's very, very fuzzy, almost like it's out of... Out of focus or viewed through frosted glass, it's not a clear image, but scientists are still excited about it.

0:02:10.8 SC: And as always, we're looking at shadows and absences when it comes to imaging a black hole. The ring is bright orange and it's swirling around a place with no light. The old image from 2019 and this new image from 2022, they're different black holes.

0:02:27.3 DC: Yeah, that's right.

0:02:28.6 SC: But they look alike. Was that expected? Were they supposed to look the same?

0:02:31.7 DC: I think it's a great confirmation, the fact that they are the same, so people are quite excited about that 'cause the two black holes are hugely different in size. The one from M-87 that was released in 2019, that black hole is 6.5 billion suns in mass, so it's 6.5 billion times more massive than our sun, and it's in a very active elliptical galaxy, and it's got this powerful jet firing out of it, so there's a lot happening and it's a very dynamic sort of situation. Our galaxy, the Milky Way, has a much smaller black hole in the center, it's 4 million suns in mass, 1600 times less massive, and it's not in a very sort of dynamic environment, there's no jet, it's a really sort of quiet place, the center of the Milky Way. Nevertheless, these two objects in very, very different situations look almost identical, and that's the confirmation that general relativity, the theory of gravity, that Albert Einstein came up with, over 100 years ago, it applies the same in whatever size the object is. So all black holes are the same, no matter whether they're billions of suns, millions of suns or tens of suns, they'll all look the same and that's what they're concluding anyway.

0:04:04.0 SC: That's very interesting. So as you say, the first black hole that was visualized this way is much, much bigger, but it's also further away. What did they have to do to kinda look closer at something smaller, what were adjustments that needed to be made on the system that was used to take these pictures?

0:04:22.8 DC: It actually proved much harder to image our nearby super-massive black hole for a number of reasons. One of them was that there's all this stuff between us and the center of our galaxy. If you think of our galaxy as a disk, we are in the plane of the disc about halfway out from the center, and we're looking inward, so we're looking through a lot of stuff; other stars, gas clouds, dust, towards the galactic center, and that scatters the light that's coming from the galactic center towards us, and so that makes it hard to get an image of what's happening right at the center. The other factor is that because the super-massive black hole there is so much smaller, things around it are moving much faster. So gas could orbit this black hole in minutes, and that means that the ring of light you're seeing, which is this orbiting gas changes from minute to minute, and that makes it very hard to get an image of it because the astronomers are pointing their telescopes at it and viewing it for hours for a whole night. If it's moving really frenetically, it's gonna make it look fuzzy. And that's one of the reasons you have this sort of very fuzzy ring in the final image.

0:05:41.9 SC: Let's talk about the telescope or telescopes that were used to take this. So this is the Event Horizon Telescope, but it's actually made up of many, many pieces, kind of like a Voltron of telescopes.

0:05:55.3 DC: Yeah, that's right. Although they call themselves the Event Horizon Telescope, they don't own any telescopes. It's a collaboration, and what they do is they book time on this particular sort of telescope, so the radio telescope, so the sort of familiar dishes that you think of for a radio telescope but they're especially tuned to look at very short radio waves which have wavelengths of around a millimeter. There are only a certain number of these type of telescopes around the world, but they need a number of them very, very far apart. 'Cause in astronomy, if your telescopes are far apart, and you combine their signals, that gives you a very fine resolution of the object you're looking at. And black holes despite being very massive are actually quite small, so they need very high resolution, and the only way to get that is to use a number of telescopes which are separated effectively by the size of the Earth.

0:06:52.6 DC: So they use different dishes that are scattered all over the place, the farthest reaches of it go from Hawaii to Spain and from Arizona to the South pole. So they just get whatever they can, and I think for that image that was released on Thursday, they used eight different observatories, but some of those observatories had more than one dish, in particular, the ALMA telescope in Chile, which has 64 dishes, which all act together as if they're one telescope. And that gives the project enormous sensitivity as well, because there's a lot of collecting power.

0:07:31.6 SC: And these data were all taken in 2017, and I seem to remember that they actually have to put the data on trucks and drive it around, they can't actually transmit it.

0:07:42.7 DC: That's true, yeah, it's recorded on hard drives because it's such huge volumes that it would be impractical to send it via data things, so they're recorded on hard drives and also they're not in a particular hurry. But the one complication of that is that at the South Pole telescope, they usually do their observing in April, and that's just as the South Pole telescope is going into the Antarctic winter, and so they can't get the drive out to the researchers. So the researchers have to wait for the summer to come again, six months later in Antarctica, until the first planes can go in and pick up the hard drives.

0:08:24.4 SC: Slowest internet ever.

0:08:26.4 DC: Yes.

0:08:27.4 SC: So once they have all the data in the same place or on the same machine so that they can analyze it, it takes a really, really long time, even once you have it all in one place. What are some of the adjustments or inferences they need to do to turn all these different readings into one image?

0:08:45.4 DC: What they're trying to achieve is get all of these telescopes to behave as if they're a single telescope, looking at one object at the same time. So there's a lot of massaging the data to try and get it into the right format and so that they're all acting as one, and then they compare the images from pairs of dishes. If you think of the number of pairs you have in this large number of dishes around the world, it's a lot of processing just to start to get to the material that makes an image, as if it was a telescope the size of the Earth.

0:09:22.8 SC: Now that we have this image, did we learn something about the black hole at the center of our galaxy, or is it more, "This is a confirmation. We knew this was there, we knew about the size of it, but we're taking a step in kind of learning more about it."

0:09:36.6 DC: Yeah, I think at the moment it's a confirmation of theory that they have shown that this much smaller supermassive black hole looks exactly the same, it's the right size. They have a pretty firm prediction of how big it should be, and the ring that they saw was very, very close to what they had predicted, so that was a good confirmation. But to learn more, they... First of all, they can do more processing on the data they have. So one of the things they already did with the M-87 image was to reprocess it to draw out the polarization of the light, so as it moves along a photon, it oscillates from side to side. And that oscillation can have any sort of orientation through 360 degrees. And if you look at the orientation of the light around the black hole, you can see how that changes in different parts of the fuzzy ring and that tells you how the magnetic field varies around the black hole. So the magnetic field around the black hole is generated by all this swirling gas, and that's really important information to understand that environment where this gas is moving very fast, it's very hot, it's a very extreme environment and it also produces these jets in many, many black holes. And people really wanna understand how those jets are powered, and they don't know at the moment, but this sort of study where they look at the magnetic field around a black hole is gonna give them some clues on how that process works.

0:11:16.1 SC: And what's on the horizon for the Event Horizon Telescope? Is it going to be pointing at different black holes, taking more data from these two? What's next?

0:11:26.5 DC: They've already had more observing campaign. So as we said, this data was taken in 2017, they've done three more campaigns since then, and the data is still going through that elaborate processing, so they haven't got any results from that yet. So that might give them some information, particularly if the look of the ring has changed in that time, but the other thing they would like to do is make movies of these sources. Now, at the moment, they just look in a narrow window in April, because that's the best time to get good weather in all these different sites around the world, but if they could look, say, every two weeks at it, in the case of M-87, which changes quite slowly, then they might be able to make a time lapse movie of how this swirling gas around the black hole moves. And that again, will help them understand that environment. But to see any other black holes which are further away, they would need their telescopes to span more than the size of the Earth, so they would need telescopes in space essentially.

0:12:38.7 SC: That sounds good. I'm there for that. Yeah.

0:12:41.0 DC: Yeah. So they would love to do it, but it's an expensive thing to do, launch space telescopes, so they'll work towards that. The goal of being able to look at all these black holes might be enticing enough.

0:12:54.4 SC: That's great, alright, thank you so much, Dan.

0:12:56.7 DC: Well, thank you.

0:12:57.5 SC: Daniel Clery is a staff writer for Science. You can see a picture of our very own central black hole at science.org/podcast. Up next, we have researcher Jason Brock. We talk about whether dolphins use concepts and labels to understand the world around them.

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0:13:19.2 SC: This week in Science Advances, Jason Brock and colleagues wrote about how Bottlenose dolphins identify other Bottlenose dolphins through sound and taste. Jason is here to discuss what this multi-modal approach to knowing which dolphin is which suggest what's going on inside their minds. Hi, Jason.

0:13:45.3 Jason Brock: How you doing?

0:13:47.1 SC: I'm good, I'm good. There's a lot to unpack here. We gotta talk about dolphins, we gotta talk about theory of mind, let's start with dolphins, we'll ease into it. Bottlenose dolphins have what's called a signature whistle, and these are unique to each individual dolphin?

0:14:01.8 JB: That's right. So in 1960s, around there, David and Melba Caldwell, working out of Marineland, Florida, had identified these sounds that the dolphins would make when they separated from the group, and each dolphin made their own different sound. For a long time, there was this debate as to whether or not there were these individually identifying calls, these signature whistles. And then probably in the 2010s, we've kinda settled that debate and really showed definitively through playback studies that the dolphins were responding to these calls as if that was an individual that they had recognized. Looking at this in the broader sense, we were really interested in this question about signature whistles from the standpoint of, Well, what do the dolphins think when they hear another dolphin signature whistle? And that got into these questions of representation.

0:15:01.3 SC: Yeah, let's talk for one second about a classic scenario where a signature whistle is used, what are the dolphins doing when this happens?

0:15:09.1 JB: So a dolphin gives the signature whistle most likely during a period of separation. If I get lost from the group, I would say Jason, Jason, Jason, Jason, until everybody either finds me or I find them.

0:15:21.9 SC: And then just any other dolphin say, Jason, back to you?

0:15:26.0 JB: They can, but that's not usually done in bouts, so we know that a dolphin is producing its own signature whistle when we see multiple bouts, like Jason, Jason, Jason, Jason. If another dolphin wants to call on me, they might say just one Jason, but then there'd be a little error in the whistle, and so they make that little mistake, usually it's some sort of upsweep or uphook into the call that we postulate, we hypothesize might be a mechanism to avoid identity theft.

0:15:58.4 SC: So interesting. We actually have a few examples here from two male dolphins. Are they involved in this study that we're gonna talk about?

0:16:06.3 JB: These individuals were not in this particular study, but they just have really cool signature whistles, so they're great to use.

0:16:12.8 SC: We'll play those right now. There's one.

[video playback]

0:16:15.1 SC: And there's the other.

[video playback]

0:16:19.6 SC: Okay, so that's the sound part, but there's a multi-modal element to this, dolphins may also be able to basically have a signature taste, and this is in the urine. My first question is not why is this urine, my question is, why is this taste and not smell? 'Cause I feel like chemo-sensing, it seems to be this domain of smell in so many different animals.

0:16:42.8 JB: In most mammals, it's really hard to tell what is gustatory from what is olfactory because these senses are so intertwined. Well, Bottlenose dolphins do not have an olfactory bulb, they cannot smell. Their nose is their blowhole. The blowhole is basically tuned to be a massive air exchange device, because of that, this meant that if they were gonna have anything in the chemo-sensory realm, it would have to be gustatory or taste-based mechanisms.

0:17:13.7 SC: In people, whenever we think about subtleties of flavor, usually smell is heavily relied on because our taste buds are... Hate to say it, but basic. Is that also the case for dolphins?

0:17:25.6 JB: We don't know. Now we know that they've lost a lot of genes related to the basic tastes that we understand, however, there's a lot of interesting work now being done in lipid taste receptors, you have your typical taste bud, and you were taught maybe that there's this area of the taste buds for salty and sweet and umami and all these others. Well, hypothesized to be kinda hanging on the top of the taste bud, is this molecule chain, basically tied to a cd36 lipid taste receptor. We hypothesize as a result of this study that perhaps it is dolphins capability to recognize long-chain lipid molecules through some sort of lipid receptor and allows them to recognize each other through gustatory mechanisms.

0:18:15.1 SC: How do we know that they are recognizing each other? What was that... The way this was shown to be an approached identification?

0:18:22.0 JB: What we did was to present them urine cues, we would do that with familiar and unfamiliar urine cues. We know how they respond to familiar and unfamiliar signature whistles in these types of setups. Eventually, you can habituate the animals or get them used to some of these sounds so that very quickly the only ones they respond to are the ones they know. Similarly, they did a lot of the same stuff for the chemical cues. I should say, where these ideas came from, because the idea of presenting urine to dolphins and hoping that they could recognize each other was a little bit of a Hail Mary. We were kinda hoping that it would work, but weren't sure only having some of the writings of some of the pioneers of marine mammal science like Ken Norris. He would highlight how sometimes dolphins would swim through each other's excretion plumes with their mouths open, this kind of highlights the value of anecdotes in science, just somebody writing this down somewhere so that it gives us ideas to look at things more systematically. But he did that, he identified that as something without it being really a structured study, and I said to my colleagues, maybe we should look into this, the signature whistles were actually the thing that was most important to us at the time.

0:19:35.0 JB: We were saying We need to really show that the dolphins understand the signature whistles as tied to identity. So we had basically said, okay, let's just see if urine is a thing, because it's a lot easier to carry urine around than it is to carry a huge high definition monitor that has to be water-proofed that you stick into the pool with an animal and hope that they can see the individual on the TV screen as we play signature whistles.

0:20:00.2 SC: Oh, you wanna show the visual. Oh, here's a dolphin. Do you recognize this dolphin?

0:20:06.2 JB: Exactly.

0:20:07.2 SC: Interesting. Okay. Yeah, sure. So is it easy to get dolphin urine then.

0:20:11.7 JB: If they know that's what you're asking for and you can train them on this, then, yes, it can be fairly easy.

0:20:18.7 SC: Oh, so you're potty training dolphins.

0:20:20.6 JB: The real trick is to tell them, "Okay, we're good, we don't need any more." Because to this day, these dolphins, if you flip them on their back ends, they think this is what you want and it flows freely. So...

0:20:35.2 SC: That's wonderful.

0:20:36.0 JB: And this is actually done for health part of their health analysis. So collecting urine isn't that strange, relatively speaking, and yeah, they will voluntarily give that quite readily.

0:20:45.6 SC: You are able to show that the same way they respond to signature whistle training, that you can do that with these urine samples, they kind of see a signature urine sample and they behave the same way as if it was a signature whistle?

0:20:57.7 JB: And so this is almost just using a different sense of a study that I already did on long-term memory of signature whistles, and so we basically just kinda copied that methodology, except instead of playing whistles, I was playing urine samples. At the end of a long pole, we put the urine in the pole and the dolphin would follow us around and we dump the urine into the pool and the dolphin would taste the urine, and we would look at how long they basically sampled the urine as one of our dependent measurements. And the way this worked out really was that the dolphins genuinely needed no reinforcement to do this, they would do this with you all day long. And that's part of why we were thinking there's something here. Because if there's nothing that they're not tasting anything, if there was nothing to this, they would just swim off and do something else. They're free to participate in this study or not participate if they don't want to.

0:21:49.0 SC: Did they ever make the signature whistle for the dolphin who's urine they were tasting.

0:21:54.9 JB: So that would be an evidence of labeling. Now, we do not discuss this in the paper itself because it didn't happen systematically, but as an anecdote that happened twice. And the interesting thing about that is we had played no signature whistles at this time, so the dolphins heard no signature whistle playbacks before that happened.

0:22:15.8 SC: That's still kind of in the realm of, "Yes, there's some evidence, but it's not systematic." But let's get into that what you do systematically here. The main experiments of the study focus on whether presenting a signature whistle and signature urine, either matching or mis-matching, you get a reaction from the dolphins that were the subjects of the study. What did you expect to see?

0:22:37.3 JB: The exact opposite of what we did see. [laughter] The only way I could explain this, to explain how they do this in like horses, for example. So colleagues at other institutions had developed this cross-modal test where you would look and say, okay, do horses recognize voices? So this is different than a signature whistle, dolphins need signature whistles because their voice changes at depth, so they have to have this kind of contour shape. You hear this kind of high frequency shift in tone, right? So the deeper the dolphin goes, there would be a change in that pitch, but the contour would stay the same. Most other animals are doing individual identity based upon voices, and so horses are just one such species. Now what they would do is they take the horses, they lead the horses in front of the herd, and they lead them into a barn, and then in the barn and they would play the call of a horse. Now, sometimes that would match the horse they brought into the barn, and sometimes it would be a mismatch. The horses that experience the mismatch would look up a little longer, "Hey, wait a sec. That doesn't make sense. That's the wrong horse."

0:23:46.8 SC: Right. Their expectations are violated.

0:23:49.6 JB: That's right, a violation of expectation. In the case of the dolphins, when you would match the signature whistle to the correct urine, that's when the dolphins would respond longer on average. And so they responded longer to the match than the mismatch, which was very surprising.

0:24:08.4 SC: What did that mean to you when you saw the opposite of what you expected?

0:24:11.8 JB: It basically said the same thing, that the dolphins are making an association with the urine and the signature whistle. The broader question of what's going on in their mind is this because the matching is the violation of expectation.

0:24:26.4 SC: Oh yeah.

0:24:27.7 JB: That could be. People would often say to me, "Well, the Dolphins have to know that you're playing a signature whistle of adult in that isn't there. They're not stupid. They can... " Well, yeah, but if I put a hologram of your grandmother or best friend in front of you, you'd look at it. Even if they're not perceiving that as an individual, here you have a more complete multi-modal representation, maybe that is the thing that is most salient to them, because now you've got two sensory systems saying, "Hey, there's an individual that you know here."

0:25:00.8 SC: Getting back to this mismatch versus match, you found that they were distinguishing those different states that when they're a match, when they're a mismatch. And that led you to say, okay, multimodal identification is likely happening. Let's get into concepts and labels, how does this fit in with what we know about the minds of dolphins, and how does this kind of support those ideas?

0:25:23.4 JB: Okay, so in 2013, my dissertation was mostly focused on long-term social memory of Bottlenose dolphins. And we did these playbacks of dolphins across five years, going to all these different facilities, and I basically... I was telephone for dolphins playing back whistles of dolphins that they hadn't seen in maybe 20 years, 20 years, a few months here, there. And we found that the dolphins responded more to the signature whistles of individuals they were housed with at one point in their lives. And it turned out that the memory was near infinite. We couldn't tell what the upper limit was, and most interestingly, I think it didn't matter how long the dolphins were together. They could form these memories for at least the call. But one limitation of that is I could not tell you for sure if the dolphin was remembering the other individual or if the dolphin was remembering the call.

0:26:18.5 JB: And now, because of this work, we can say that they do form representations around signature whistles and their use of the signature whistles essentially function the way labels do in human names. So if I say the name of my mother or my father and I say that to my sibling, they're recognizing almost like they have a picture of my mother in their head.

0:26:42.5 SC: You're bringing up a concept, you're calling to mind a specific thing rather than, "Here is a name, let's talk about this name."

0:26:51.5 JB: Yeah. It's a noun usage fundamentally.

0:26:53.7 SC: And is this something that's been seen in other non-human animals?

0:26:57.8 JB: Most animals, when they're using sound to represent identity are doing it through a voice cue, because dolphins are innovating signature whistles, they're innovating and developing this. They represent a very rare group of animals using, basically, an arbitrary name that they have come up with or an arbitrary signal that they've come up with to represent their social identity, even Orcas. We think more run on group signatures than they do on individual signatures, which has all kinds of implications for how they might perceive identity and self, so that's a really interesting concept that needs much more study. Belugas, who are the canaries of the sea. We know incredibly little about what all those calls mean, and whether or not they even have a signature, it's just so much to them. The thing about signature whistles are they've been studied for a longer time, and we have a better handle on them than anything else, so that's why we were able to make this leap. But would it surprise me if we find over time that other species, and even especially crows and ravens and other corvids can do stuff similar to this? It wouldn't surprise me if we find out they can.

0:28:13.8 SC: What do you see as the next big questions? The next steps to take with this research to solidify what you have here, or to expand on it?

0:28:22.2 JB: Generally speaking, there's two ends to go from this. Now that we understand that signature whistles really are representational, we know that we can use these as a stand-in for that individual, that opens up a whole new realm of cognitive studies. Do you associate this individual as a relative? How does kin recognition work with signature whistles? Are there codes for last name somewhere in the whistle that you have to figure out? Some other ideas: What chemicals are in here? How does the exact gustatory mechanism operate? What excites me the most about this from a physiological point of view, and again, this started as a, "Hey, we wanna know about dolphin minds and whistles." So the next step might be to say, "Okay, if this is a CD36 lipid taste receptor," and we know they have them, and we know that whatever use they have in dolphins is preserved from the bovine lineages, the cows that have CD36, whatever cows are using CD36 for is pretty much the same function is what dolphins are using it for, so are there other species that can do stuff like this, hippos, giraffe? We know giraffe does a lot of urine tasting around reproductive assessment, are dolphins using it for that purpose? Then that might actually be the origin for this whole thing, males really needing to understand when females were reproductively competent.

0:29:45.3 SC: Very cool, thank you so much, Jason.

0:29:47.9 JB: It was a pleasure. Thanks for having me.

0:29:50.2 SC: Sure, Jason Brock is an assistant professor of biology at Stephen F. Austin State University. You can find a link to the science advances paper we discussed at science.org/podcast. Next, we have a custom segment sponsored by Michelson Philanthropies. Custom Publishing director, Sean Sanders chats with philanthropist Gary Michelson about why funding agencies need to re-double their support of immunology and immunotherapy research.

[music]

0:30:26.3 Sean Sanders: Hello to our listeners and welcome to this Custom-sponsored interview from the Science AAAS' Custom Publishing office, brought you by Michelson Philanthropies. I'm Sean Sanders, Director and Senior Editor for Custom Publishing at Science, and I'm pleased to have the opportunity today to interview Dr. Gary Michelson, founder of the Michelson Medical Research Foundation and [0:30:48.2] ____, together with his wife, Alya of Michelson Philanthropies. Dr. Michelson is a board-certified orthopedic spinal surgeon, a serial inventor with nearly 1000 patents across the globe, and the founder and funder of three private foundations. Michelson Philanthropies has partnered with Science and AAAS to support a price for early career scientists, known as the Michelson Philanthropies and Science Prize for Immunology.

0:31:16.8 SS: It is with this in mind that I'd like to welcome Dr. Michelson to a conversation about the importance of immunology research, why it is critical to be funding such research and which areas of immunology he feels are most in need of support. Dr. Michelson, welcome.

0:31:35.5 Gary Michelson: Thank you, Sean.

0:31:37.5 SS: So my first question for you is, with all the critical fields of research out there that need funding and could benefit many people through their support, why immunology?

0:31:45.9 GM: The history of medicine has been what I would call reductionist, you pick a disease, and you start drilling down, you get an answer, and then you drill down beneath that, and Hannington's career is really one of the best examples. They drill down to the molecular level and actually found out that the entire disease is caused by the substitution of a methyl group for a single hydrogen atom. What's more interesting is that gene editing offers the answer to that disease and every single other hereditary disease, so this concept of there's one big answer for a lot of problems, non-reductionist, whole systems kind of answers. And my answer to your question is, immunology is the science and the study of the immune system, its application is immunotherapy, and I believe it holds the answer to almost all human disease, because every disease that I look at that kills people, it's the immune system at work or failing to work properly.

0:32:47.0 SS: So the field of immunology has achieved many breakthroughs in the past two decades that were unimaginable previously. Could you highlight some of these advances for us?

0:32:58.0 GM: Sure, the most significant would have to be the new method of developing vaccines, which was broken with 3000 years it came before it. 3000 years ago, the Chinese were lansing pustules from cowpox inoculating people against smallpox, and we recognize that Jenner did that in 1790, and of course were advances in vaccine development in the 1860s, from Pasteur. But up until five years ago, that's how all vaccines were basically developed on a one-by-one basis against a virus or a bacteria. We've invested 30 or 40 billion dollars, and have not succeeded in developing good vaccines against tuberculosis, malaria or HIV. Now, in the last five years, we finally tried a different approach to vaccine development, and that is to create a cassette player and insert into that a cassette the genetic sequence, the codes for some marker of the virus or the bacteria that we can react to...

0:34:03.6 SS: And this cassette that you're talking about, this is the mRNA technology from Moderna and Pfizer is that right?

0:34:09.8 GM: Right. And that's allowed vaccine development to leap way ahead.

0:34:14.5 SS: So what do you imagine the field of immunology will look like over the next decade, and what do you hope to see?

0:34:21.9 GM: Well, the progress is gonna be revolutionary, not evolutionary, and I think this will be the decade for that, because the very first things that will happen is we will set ourselves upon the task of actually inventing the tools and the methods by which one can study the immune system.

0:34:43.8 SS: Immunotherapy treatments are still quite new and expensive, and are therefore limited to wealthier countries, and those of means. What needs to happen to bring these treatments to scale and make them more accessible to a broader population?

0:35:00.0 GM: I think we'd better begin with, what's the definition of immunotherapy? It's really just the medical or therapeutic application of immunology, and somehow it seems to become synonymous with cancer treatment, but it really isn't. It's much bigger than that. So to begin with, it's still active vaccines again, which are clearly the most effect, most bang for the buck of any medical treatments. Now, if you're talking about cancer immunotherapy, so to begin with, there would be check point inhibitors, and those can be produced relatively inexpensively compared to, for example, CAR T. The problem with CAR Ts are they are vaccines, they're just an individuals vaccine that are produced on a one-by-one basis, and there are efforts in progress right now to develop off-the-shelf universal CAR Ts, which would drive the costs down tremendously.

0:35:51.2 SS: Could you explain just briefly for us what CAR Ts are?

0:35:56.0 GM: Presently, it's when you extract from a patient their own T cells, and then you genetically modify those by form your chimera, that's more potent than the original T-cell was you re-infuse that into the patient as a one-time vaccine, it hunts down the cancer cells and kills them.

0:36:12.9 SS: Ground-breaking discoveries today are seldom the work of single researchers, but rather require teams of workers often across many disciplines. How can interdisciplinary corporation be improved and enhanced to more quickly bring breakthroughs from bench to bedside?

0:36:29.0 GM: Let me not only agree with you, but give you a beautiful example. So we founded a medical research center at USC, and there's a gentleman there named Peter Kuhn, who's a researcher, and his area of expertise is a liquid biopsy for cancer. Now, the diagnoses of pancreatic cancer is pretty bad, because by the time you discover it, it's too late to do anything about it. Now, if we could have early detection of what are called occult cancers such as pancreas or may be kidney, may be far more curable. And what a liquid biopsy does is it actually looks in the blood for either genetic material from these occult cancers or protein products that only they produce. Now, the liquid biopsy actually required the coordination of physicians, medical researchers and scientists, photo optic engineers, computational scientists and engineers could actually build the machines.

0:37:31.0 GM: Now, the problem is that most science in academia today is funded by NIH, and what they do is they fund essentially one out of every five research proposals, setting every scientist in competition with every other scientist. What they don't do is fund science on a project basis, like the Manhattan Project. And so what we need to do today is to de-silo these brilliant people from all these different areas and have them work on projects together. What we need to do is something that's never been done. We need to build a field of dreams research center on the same scale that industry would. A 500, 600 scientists center that the greatest breakthrough in recent times in all science is big data, but as I like to say, big data is like sucking on a fire hose, you have to have a computational scientist, you have to have pattern recognition, you have to have AI, deep machine learning to make sense to that. Well, those guys certainly don't talk the same language as a molecular biologist. We need to de-silo these brilliant people, have them live and work together on a common project.

0:38:47.6 SS: What do you think will be the most critical challenges in immunology that we're going to face in the future?

0:38:53.5 GM: They're immediate, they're the ones right now that the Burnham Institute, they are cloning human heart cells that are sitting on a glass slide, and every day they test chemicals on these living beating heart cells. We have no ex vivo human test bed for immunology. So the very first step is to create one of those, we have to have an ex vivo test system. What the opportunity and the challenge is right now is to invent the tools and the methods by which we decode mysterious workings of the immune system. You know, I keep making this point, two economist out of Harvard, one year into the COVID, pandemic did some calculations and said that the first year of COVID cost the United States economy 17 trillion dollars. Now, if 17 trillion dollar hit the economy is the fire, what would the fire insurance look like? Well, maybe it would be reasonable to invest, let's say three or four, or five percent of the Gross Domestic Product of the United States into scientific research. It would be the fire insurance that we don't take another 17 trillion dollar hit, and there are far, far worse bugs out there than COVID, we really better up our game.

0:40:10.6 SS: Dr. Michelson, thank you so much for making the time to talk with me today. I trust that your work and that of the Michelson Foundation will continue to drive immunology research forward.

0:40:21.0 GM: Thank you, Sean it's always a pleasure.

0:40:22.5 SS: Our thanks to Michelson Philanthropies for its support of the Michelson Philanthropies & Science Prize for Immunology and for making this conversation possible, and of course, our appreciation to the Science Podcast audience for your interest and attention until next time.

0:40:42.0 SC: And that concludes this edition of the Science Podcast. If you have any comments or suggestions, write to us at sciencepodcast.aaas.org. You can listen to the show on the Science website at science.org/podcast or search for Science Magazine on any podcasting app. This show was edited and produced by Sarah Crespi with production help from Podigy and Meagan Cantwell. Transcripts are by Scribie. Jeffrey Cook composed the music. On behalf of Science Magazine and its publisher, AAAS, thanks for joining us.