Neurobiology in a Changing Ocean

Martin Tresguerres: My approach to science is to really be curious and doubt everything. If you have the right curiosity and right tools, you always come with exciting questions, so it never gets old. It's always something new, something exciting and just sometimes thinking that I am the first person in the history of the world to think about these things or to see these things is really, it's very thrilling. I am Martin Tresguerres. I'm a professor in marine biology at Scripps Institution of Oceanography at UC San Diego. Teaching is another integral aspect of science and of my job, and I do teaching and training at different levels. For example, for undergrad, something that I love doing is putting a little bit of that seed of curiosity, that sense of wanting to know more, because you can always ask or answer a question to a certain level, but then you might be happy with that answer.

But I want my students to go further until they reach that point in which there's no answer. Ification, ideal surface area, and also something that we haven't seen so far is all respiratory surf. Really, I love my work, but it's really time-consuming and very intense. When I get off the lab, I really try to maximize the time with my family, my wife, Thalia, my daughter, Maya. Try to do as much activities, spend as much time as I can with them. When I have the chance, I still play basketball.

I grew up playing basketball in my hometown. I was part of multiple teams ranging from my hometown, the university, during high school, and even here. I see sports and especially team sports as having a very influential and important part in my formation and in my career. I really like having this community of people trying to achieve a certain goal, which I learned from my home club. I love having that idea of division of labor, but all for the same goal. I try to apply even though I'm not thinking about this all the time, I think I intrinsically try to apply these principles to my work, my lab, and my collaboration. I was born in Rio Gallegos in the south of Argentina, and I grew up there.

So this is one of my favorite pictures from my childhood. I must have been maybe six or seven years old. We're there, it looked like in the middle of nowhere. Well, that mountain that you see in the back is called Chalten. Also known as Fitzroy. That is actually the mountain that is in the logo of the Patagonia, the outdoor clothing brand. That place happened to be maybe it's like three, four hours away from my hometown. So we used to go there a few times a year, maybe often enough. I just love this picture. You can see there my mom, my sister, and my brother, and my dad obviously took the picture. It's one of my favorite places in the world. I would say the hardest part of my job is being away from my family during extended periods of time, and this goes into different levels.

For example, in Antarctica, I went away for six weeks, and not being close to my wife and my daughter was really hard. It was the only hard part of that trip, to be honest. Even though you have FaceTime and other things, it's just not the same. Then at a different level, living in a different country from my mom, my brother, sister, and my friends, I have a very close group of friends or several close group of friends, and that's the one thing I miss about Argentina. I go over there every time I come, but it's not very often, unfortunately.

But every time I go, I really try to embrace it and enjoy it as much as I can, because those moments are really precious.

Panama was one of my favorite experiences in my scientific career. If I had to pick another one. I would pick my recent trip to Antarctica. That was a trip that I did with Alison Murray at the Desert Research Institute and Bill Murray from University of Southern Florida. It was just like a Discovery Channel type of work. We were on a ship for five weeks. Constantly, we were doing cutting-edge experiments, including gene sequencing and microscopy experiments on board. So that in itself was amazing. Plus, scuba diving, mini submarines to scope the environment.

Then on top of that, the work itself was just absolutely amazing in many aspects. The scenery is just, like, it's fantastic. It's difficult to describe being there, immersed by icebergs, ice, glaciers, whales, penguins, seals, leopard seals, orcas. The project was started by Bill Baker and Alison Murray maybe 10, 15 years ago. More recently, the three of us together, we got funding from the National Science Foundation that supported our journey to Antarctica, as well as all the further experiments that we are going to be doing for the next couple of years. Welcome to the Jeffrey B Graham Perspectives on Ocean Science Lecture.

Wow. Welcome, everybody. Wow. That makes me I watched that video three times, and I cried five, I think. Yeah, thank you, Michael, for that great, great video. It's just absolutely great pleasure to be here at Birch Aquarium. It's one of my favorite places, and it's a special honor to be part of this Jeffrey B Graham perspective in Ocean Sciences. Some of you know Jeff was my mentor when I was here. He really changed my career, my life, and I miss him dearly.

But what I really want to tell you about today is about this Allen Discovery Center for Neurobiology and Changing Environments, or ADC-NiCE. This is a big project funded by the Allen Family Philanthropies, and it's really a team effort that with 13 labs, you see here from UCSD, from Scripps, UCSD, and a few other places around. We started about 17 months ago, and it's going very, very well, and I truly think it's one of the most promising tools and projects that we have for trying to do something about changing environments and climate change.

This project is centered in the neurosystem on neurobiology, and there's a very good reason for that. When we're talking about changing environments and climate change, there's so many things. But then if you have to focus on one, it would be the

nervous system. The reason is that the nervous system really is the interface between animals and their environment. You can kind of see here even though this is a still photo that I took in Cabo Pulmo in Mexico, you can see there how there's, like, life is so dynamic. There's lots of interactions, the animal trying to get other animals, looking for food, escaping from predators, sensing chemical things, vibrations, light. When we try to find something that can be very relevant on many, many aspects, the nervous system is the top choice.

Then on top of that, as we all know, the world is changing; humans were changing our environment, and some of the things that is here, warming, acidification, low oxygen, which is known as hypoxia pollution. All of those things have the big thread of affecting many of these systems, but it's very difficult to know exactly what and how, and to forecast and to try to find solutions when we don't know how the nervous system of these animals work. Believe me, we know quite a lot about humans. We know quite a lot about mice and seal fish and a couple of other model organisms for biomedical sciences.

But when it comes to real animals in the real world, we know very, very little. I did a very quick calculation, and we probably invested less than 0.01% of all the money we have put in biomedical sciences to similar aspects of marine life. On top of that, there are thousands and thousands of species, and the environments are variable themselves. So with that, it's on one hand super important and critical, but then it's also very challenging. So how do we even go about that to try to do something about that? The idea we came with is a transdisciplinary team, which is ADC-NiCE. To tackle this from different aspects, we designed four different what we call research spheres.

One of them is called neuroncytognomics, which is basically genes and cells, looking at the cells and the composition, how the cells of the nervous system works. The second is neural activity. So looking at neurons working in real time and how they might get affected by a changing environment. Then going into physiology and behavior to make sure that the things that we look in great detail under microscopes it is relevant for the real animals. Then finally, these environmental neurogenomics, which is to bring everything together into the larger picture in the environment and under the light of evolution with population genomics. You see here we are 13 labs. We also have engineers and people who can do more like integration across spheres through modeling and other sophisticated techniques, which I call magic.

Altogether, by going with all this transdisciplinary approach, we're making great progress we're going to tell you about tonight. Now, our goals and our mandate, our aims are several-fold. It all starts with developing innovative tools and methodologies to study marine environment or the neurobiology of marine animals. Again, it's not the same studying a mouse and studying a coral, and we need to create the tools, and we are creating the tools to look at these details in this process in great detail. Then something that is the second one would be to reveal or discover, if you want, fundamental biological mechanisms that allow animals to live and thrive in naturally changing environment. The environment can change naturally due to tides and different cycles, and animals are living there. We know very, very little about how these animals do it. That's the first goal, to then be able to see what would happen when superimposed human-induced climate change might affect the medium further.

This one is critical as well. Maybe you have heard about something called AI. It's a little popular recently. Well, AI is great if you have the data and the foundation in which you can tell AI to predict things. But guess what? We don't know much about corals. We don't know much about these snails or sea urchins or sticklebacks. So if we let AI do their modeling with the information we don't have, they're going to come with something somebody once said, for every complex problem, there's a solution that is simple and wrong.

Then, going back to these four spheres, there is a lot of existing genetic diversity in the world. There are different populations of animal living under different conditions, and that existing diversity. If we understand it and we can see what it's for and what it might be better at, that's a huge source of hope to be able to find solutions. Then maybe at a larger scale, in addition to the work that we're doing ourselves, we are catalyzing scientific policymaking and public management around environmental neurobiology. A big part of what we're doing here at the Birch Aquarium. I'm going to tell you more later.

But it's a little bit going behind the idea that if you get, especially neurobiology sounds very intimidating, like it did to me. But if we get kids from an early age, saying, neurobiology is related to how maybe a fish might see and trying to make it bring it down so it's not that scary, we can bring more people into this project. Then finally, in the medium term, hopefully, maybe earlier, is to really our information; we hope that it can inform science events, interventions, conservation strategies, and policy making.

Now, all of these sounds very, very a lot, to be honest, when we wrote this project, I think myself and everybody in the team was like, oh, that's great, but how are we going to do that? It's working surprisingly well. One of the key aspects is, instead of focusing on one animal is to focus on four animals that are very different from each other: a coral, a snail, sea urchin, and a stickleback fish. So that is called biogenetically diverse, and that means that they have different patterns of neurobiology. We don't know exactly what those patterns are, but we know that the complexity is different. They are sensing different things. And then by having this diverse array of experimental individuals, we hope to be able to look at specific as well as broad mechanisms with relevance for changing environments. They have increasing level of nervous system complexity, ranging from more like diffuse network of neurons to ganglia, to then a brain, like in the fish, just like humans.

And then two very important aspects here is like one, these animals are ecologically important by themselves. And corals, we don't even have to explain they form coral reefs, and they are the foundation of the most biodiverse environments in the world. The snails are also very, very important from trophic chains. There may be invasive species. Sea urchins are known as ecosystem engineers because they can manage other algae and in forests and coral reefs. And the sticklebacks are also

around the world, and they're very important for different trophic chains.

So we're not studying like a fly to understand humans. We're not studying like a zebrafish to look at something. Whatever we find here is relevant directly to the ecology of these animals and to the world. Then finally, even though there are what we know as non-model organisms that are difficult to work with, we have many tools which are in the large part created by people from our team to do more fancy or sophisticated genomic manipulations and sophisticated microscopy techniques. The first sphere, then I'll go sphere by sphere and then see how they can get integrated. We call neural cytogenomics. There's a lot of fancy word there, but the core goal is to look at the cellular organization of the different nervous systems of all these animals and how it might react or respond to changing environments. You see here some of the things that we're looking at, genomic responses, neural maps, transgenic animal models.

Just to give an idea here, because I get this question all the time on neurobiology of corals. Like, what are you talking about? The thing with corals is that even though they might look like rocks or like plants, they're animals, and they create these amazing ecosystems. But if you go deep down into what these things are, they're just created of cells like any other animal in the world. You have these tiny little they call like polyps or tiny little anemones that are connected to each other. They have a mouth, they have a gut. They make the skeleton or the reef is underneath.

Another area of my research is trying to see how they actually do that. But they respond to the environment, they tune their physiology to the moon cycle and other things. Yeah, they do have a nervous system. We do know about the nervous system from related animals, little hydra, which are like these freshwater, tiny, polyp-like creatures or sea anemones, but we don't know much about corals because they're very difficult to study. It's just difficult to put a chunk of rock in a microscope.

But we've done very good advances in the past year and a half or two. This is work. These are beautiful images by Dr. Claudia Tatiana Galindo-Martinez, or Tati. [Laughter] But when it comes to corals, and then you see here, I have some of the members of the team which are involved in one way or another, really like a team effort. What you see here, this is one of those polyps seen from the top. This will be the mouth of the polyp. The green is they're fluorescent, the corals are fluorescent. The red are the symbiotic algae that lives. Each of these tiny little dots is an algae, and the yellow signal that you see there is a label for a specific type of neurotransmitter that is important for corals and other invertebrates, but it's not important at all in humans. Just to give you a glimpse of what we're seeing here, again, in greater detail, we see algae, the symbiotic algae which are living inside the cells of the coral.

Here in this image from Tati, you can see the label showing neurons or neuronal cell from the coral that are in close proximity to the algae. Well, we don't know exactly what it's doing, but it's revealing. This is an example where you don't know what to expect or what to investigate until you see it. Now this is shifting into maybe neural control of symbiosis in corals and other animals. Implications for bleaching, perhaps, we still don't know.

Now, this is very recent data from Dede Lyons's lab. She is here in the audience. Hi, Dede. What is showing here is a snail embryo developing in real time. If this is the adult and this is about half an inch, this would be more or less up to scale. In this case, we are just going to fundamentals. I'm going to just play that again. How do they build the nervous system? This is a mollusk. It's very, very different from a vertebrate like a fish, a human, or even like a coral.

Going back to the same principle, if we don't know how things work in the first place, it's very difficult to pinpoint what happens when things go wrong. We don't know much about mollusks and this type of work in high resolution, high detail, is going to be very foundational. Then from there, we can start seeing does climate change or certain aspects of climate change affect neuronal nervous system development in snails and related animals. But if you don't know how it happens in the first place, how are you going to know what happens if anything goes wrong?

The next sphere is called neural activity, and then here we're going to see neurons working in real time, trying to see patterns and trying to see how all the information gets integrated. To be honest, three years ago when I started putting together this center, if you told me we are able to do this, I would tell you that you're lying. I cannot tell you how much I've learned during the process of writing the proposal, interacting with all the team members and now doing the work. A lot of this work is spearheaded by Matt Lovett-Barron who's also here in the audience. These are results that he had previous to ADC-NiCE. This is a zebrafish larvae. It's attached here under the microscope. You can see eye movement, heartbeat, and other like tail movement.

But what you see here is kind of like [inaudible]. Each of these dots is a neuron, and the neuron, they have a transgenic reporter that when the neuron is active, it flickers. That flickering that you see there is the brain of the zebrafish larvae just leaving. What is equally amazing is that Matt and his team, they're able to not just see this super pretty image, they can also try to understand based on which areas of the brain they get light up under different conditions. Let's say you put a smell, these neurons light up, you play sound, something lights up, and then track that and then establish patterns about how the integration of signals from the environment into the brain, into, let's say, that's the smell of a predator. Let's just swim away, and then you can track that in the brains, in the neurons, and then that might respond, for example, in the tail moving faster.

What we're trying to do now or doing is looking at similar techniques, similar methods for other animals. This here is a sea urchin larvae. It's from Amro Hamdoun's lab. They're doing just amazing work with this system of sea urchins. These larvae swimming freely in a stage, and each of those glowing dots is neurons from the sea urchin larvae that you can see they're like responding, and we still don't know what they're doing, but we can see it. Then if you can see it, you can try to understand it

better, and you can try to test it and see if it gets disturbed by, let's say, ocean acidification or warming. Amro and Chloe, Nathan Shaner, Gerry, they're all working together from different labs, and it's just very cool to see how this idea of having teams working together, it's actually working.

Then another really nice thing about this system is that Amro is developing these things so you can study not just in larvae, but also as the animal grows and try to go all the way to adults. This is an example of that. Now, if you have that larvae, the larvae grows, this is more or less up to scale. This is the next stage, and you also see these neurons working. What I've been telling I'm a broken record, but it's true. First we need to develop the tools to be able to see how things work and then see how they may be affected by environmental change.

Now the next sphere is about behavior and an physiology, going back to that idea that, yeah, you can have some cool trick in the petri dish, but is it relevant for the animal because if it's not, it might give you a bunch of papers, but really, who cares? So here trying to focus on key sensory modalities, which in plain words, it means like hearing, visions, smelling, vibrations, and then see whether those things that we look at great detail at the genes and at the cells are important for the animal.

Another great example of collaboration between labs, this data from many people like Rose, Devin all under the umbrella of Matt, who's also collaborated with Brian DePasquale and Brady Weissbourd through a Scialog project. The concept that I want to convey here is that sometimes things are more difficult than what you'd imagine. For example, let's look at fish behavior and let's see if warming affects fish behavior. How are you going to do that? Are you just going to look at the fish and say, yeah, it's moving a little bit faster, I think? We need to create the tools to analyze that in an unbiased manner, and that's precisely what it shows. Each of these is a fish that is moving. What I haven't told you yet that this is at lower temperature than that one. In addition to be able to track that automatically and obtain a bunch of information about speed, localization, and other things, this can be analyzed.

When you put all the data together, and this is preliminary, but I just want to give you a glimpse, what you have here I believe it is at 17 degrees Celsius, like 65 or so Fahrenheit, and then this is five degrees higher. You can start seeing patterns in changing in movement of this schooling of fish. Are the fish getting closer or not? Are they moving faster, not moving faster? At this moment, we don't say if this is good or bad, doesn't matter. At this moment, it doesn't matter. The important thing is that we can measure that and we can quantify it, and then when we start doing our treatments, you can see if something is different or not in an unbiased manner.

Then one of the goals is going into more complex behaviors because I know all of us in ADC-NiCE we got into this because we loved what the animals do in the real world, and I'm sure you guys are here for the same reasons. The Birch Aquarium, if they had a couple of fish going around, they probably would croak in about 3.5 hours. You're seeing the animals in action. This is something that Rose took the lead here looking at this is a stickleback fish. In this species, the males, they actually build a nest, and the female they will come afterwards lay eggs, and the male is actually the one in charge of doing the parental care. We have no clue how to analyze it yet, but it's just to show that we are hoping to go and then go from simple test that might tell us something into trying to find a way to study, analyze, and have a better idea about real behaviors in real environments.

Now, for fish, it might be easy to imagine, like we can do a bunch of different tests. Fish they do lots of cool things, easy to see, but how do we do this for corals? We're studying adult corals at different stages, but we have a special attention or a special interest in coral larvae. To give you an idea, this is a video from Reef Patrol and SECORE International. They allowed me to show it just to show that coral larvae are key for coral reefs. In general, larvae and early life stages are essential for populations of marine invertebrates in the world because you have millions and millions of embryos that are going to be floating around. They need to go and find a place to settle and grow. You start with millions and only a few are going to make it, but that gives a lot of hope because there's a lot of genetic diversity.

If we can improve coral recruitment by just a minimum amount, the chances of helping with coral reef restoration are huge. These are the coral larvae. They're going there, sniffing around where they can settle, where they cannot. You might be surprised, but we know almost nothing about how they do it at the molecular level. It will be equivalent to say, we know that humans can hear, but we don't know how well they hear. They like this song, but we don't know how they sense it.

Well, that is equivalent for coral larvae, we do not know. To take a deeper look about how these things might look, this is a coral larvae in our microscopes. They are far from being particles that are very passive. In fact, they are covered by these little hairs called cilia, and the cilia allow them to move. As we are going to show you next, these are very complex structures that are probably just sensing and tasting and doing lots of things by mechanisms we still don't know.

But they are probably involved in deciding where the coral larvae settles and therefore, the fate of coral reefs. We start by characterizing the nervous system. Again, Tati's images here showing these are neuropeptide FMRFamide that is, again, important for invertebrates, but not for vertebrates, not for humans. Normally, you see a coral larvae, like in the video I showed you before. This seems like a little thing like maybe some cells. I don't know. You go deeper and deeper, and it's a very complex network of neuropeptides, which is sending signaling, sensing, telling the larvae what to do. This is just one of them. They have several of these neuropeptides. If you take a closer look what we see, and we were not the first ones to notice this, but what would be the front of the larvae, this is the part that is swimming forward, is especially enriched in certain neurons that give the idea that they might be sensing the environment and allowing or telling the larvae to swim that way.

We're tackling this with some more like sophisticated tools that until relatively recently were exclusive for biomedical sciences,

mostly because of price. These things are expensive. But also things are more complex. It's not the same to work with cells from marine animals. You have to work with seawater and you have to optimize things, and at the end everything gets super expensive and you can ruin the career of a PhD student or two because it takes too long. But the Allen ADC-NiCE gives us the resources to actually do it. This data from my PhD student in my lab. To simplify this, what we're doing here, we're looking at gene expression. Each cell or many cells of these coral larvae, we can look and see which genes are expressing at any given time.

Then by looking at those patterns we can deduce maybe these cells are neurosecretory cells are secreting neuropeptides. These might be what are known as mechanosensory neuron, they're sensing movement. Peptidergic neurons or mechanosensory neurons too. You also have other cells lodged in the skin or stem cells, and this is just like a representation of the genetic expression of each cell type at any given time. Which is very handy when you want to characterize neurobiology in something new. Then you can go into more detailed studies. Don't worry, I won't go through all of these, but what I want to show here is that this specific cell type expresses these three genes.

One of them is called Otoferlin, CA1G and ATS6. In addition to see what genes are expressed, we can visualize where in the larvae these are expressed. I want you to pay attention especially to this one because Otoferlin you can see how it is mostly in the anterior part of the larva, the larvae is swimming that way. When we look at what this gene might be doing, it might be related in humans if you have problems with Otoferlin you are going to be deaf. It is intrinsically linked with sensing vibrations and sounds.

Then the other ones are also genes that are seen in hair cells in the ear involved with hearing. Now, you might have heard there is some evidence that the sound of healthy reef may attract coral larvae or that they might be able to manipulate larval recruitment by playing different songs, which would be great. But now, the mechanisms are very unknown, and we don't know if Otoferlin is involved in that, but it gives us something that we can test. Instead of trying 3 million different sounds, we can go and see if this gets affected in one way or another, fine tune it in the lab, and then that can greatly expedite trying to find or use sound for larval recruitment, for example.

Well, that takes us into the fourth sphere, which is environmental neurogenomics, and it's in one word or in a tagline, it will be identifying genomic signatures of adaptation. Existing genetic viability that already exists in natural population that might indicate resilience or susceptibility to changing environments. Then the other part of this, the flip part of that is okay, trying to do experiments that reflect that environmental variability that is seen in nature separately or independently from climate change. To that second part, something that we proposed originally, and we completed in record time, actually is this work by Todd Matts and Taylor Reeds. They just put together these machine. We have one here, the other one there. What these machines can do is they can simulate any combination of pH, oxygen, and temperature in real time to simulate any environment that you want.

It's because then when we have our fancy sea urchin or coral larvae that is glowing and showing the neuron, we want to see how they respond to changing environment. Well, you need to be able to generate that changing environment in the first place and this is our tool. I still remember when I asked Todd if he could do that, and I was like, Todd I have a question for you. I know you're very good. You do a lot of things with sensing the environment, but could you do an equipment that does that, this and that? He looked at me and was like, yeah. We want to do this. I already have one of those. I use it to test my sensors. It only goes to the third decimal point after the pH. Would that be okay? Okay. Great. Then the challenge was to make this user friendly and deliver this, so it's just a little more complex than that.

I'll show you examples of how this can be so important. This is the sensors right at the tip of the SIO Pier, and what you show is pH, oxygen, and temperature. If you look at the solid line, those are variations in these three variables that you can see normally every day as a result of photosynthesis and respiration. We're talking about or we're concerned about ocean acidification in which pH of the ocean might go down to 7.8 in 100 years. Well, a descript fear if pH can go down to 7.6 overnight and animals are there. Oxygen go there from 150% saturation due to photosynthesis to almost hypoxia and die. This is independent of climate change. Changes in temperature from like 20 degrees Celsius to 18 in 12 hours.

Then what you see in the dotted lines, this is our pHOTEC system mimicking those environments. We can just put our animal not have to go to the Pier because in the Pier you cannot measure neurons glowing. We can put them under the microscope, simulate that, and then see what happens. Do they sense smells the same way? Do they sense a hearing cues or chemical cues? You can do anything here. This is Kelp forest. I think it's outside of Hopkins mining station, changes in pH, also the swings. They're very abrupt, but also they're not necessarily predictable, oxygen, temperature. Todd is upset because he says system cannot simulate exactly that. I told him it's okay. Coral reef and even within a coral reef depending where there are changes, these things are more variable even within the same reef, but this change in pH is more like a diel type of day night cycle and can also simulate it perfectly.

I took this video last week. Actually is Matt White, again, a PhD student who we are co-supervising with Matt and Diana. This is fantastic. Just to make sure that it worked correctly, there's a little fish in there. We are using the pHOTEC to change the different conditions. Then you will see that here in the screens, this is how we set the parameters, and then that is the fish and looking at, do they move the pectoral fins more or less? What happens with heart rate, what happens with the gills and the opercular movement?

Then from there we'll move into the other animals and the neural activity and so on. But then, of course, when you're talking

about adaptation and responses, things happen in longer than a week or a month or a few hours. It happens over thousands of years. To look at that we have two team members who are just experts on this. One is Diana Renson here from UCSD in Biological Sciences. The other one is Carly Genkl at USC. Diana studies stickleback and Carly studies coral. The idea here is to just take advantage of nature, which is the greatest experiment and the longest running. Hopefully, we can keep it going. What we have here is for these little fish, the stickleback. There are different populations ranging from California all the way to Alaska. They are the same species. These are not different species.

They're the same species. If you see here, the difference in temperature, at least in mean temperature, it could be over 20 degrees. The animals are there. They're smelling, they're seeing. They're sensing. They are there. What makes a stickleback from California being able to operate at warmer temperatures than the one in Alaska and vice versa. To do this, and I'm not even going to try to explain it in detail, but what you can imagine here is each of these is a chromosome in this stickleback, and then each dot is a region of the genome or of the chromosome, and the yellow dots are things that show some signature of adaptation or some mutation that is beyond that of chance, which suggests that there's a linkage between that trait and the environment. This is from the population from California. This one Haida Gwaii, which is in Vancouver Island, you can see that even though they live a very different temperatures, you have areas in Canada and in California that have changes in temperature because they might be closer to a certain current or a certain side of the island.

Something that is very exciting is that the yellow dots are parts of the genome that have similar mutations between the two populations, which to put it in simple words, this technique which is called GWAS might allow us to look at signatures of adaptation to warming or acidification or different conditions in existing populations.

Now, how do we put all of these together? Because I sold the Allen family philanthropy the idea that we're going to work all of these together. I'm just going to give you two examples. With stickleback, this is how we integrate the spheres. We have the sphere that is looking at cells and genes. These are the single cell RNA-seq or the gene expression in adults, juveniles, we're also looking female, males and other stages. Then with this one we are establishing which cells express what and what are the different neural types in the brain.

Then with the type of work that Matt does and we're expanding these tools into stickleback, if we see some interesting genes in specific, let's say, these cells they seem like they are involving vision, we can go and specifically see how they work. We can see how they work with warming temperature. We put them in the pHOTEC and we can see if that gets affected or not because they might be able to buffer the change in the environment and then connect it with the behavior at different scales, heartbeat rate, opercular movement, schooling, building a nest and so on.

Then finally we can go and see if some of these genes and mechanisms they present any signature of selection in the populations. Then what is super exciting here is that we can go in each direction in this diagram. Let's say we see a gene that is interesting from this point of view, maybe related with vision, then what happens with that particular gene? What happens if we knock it out? Or what happens if we put this gene from a warm population to a cold population? Do we make them more resilient? Does it affect the next stage? This arrangement is very dynamic. It can go in each direction, and it can generate hypotheses. It can help us plan experiments, and then it can help us find answers. Then, of course, we'll go into the next hypothesis and the next experiments and the next answers.

With corals, and then this is probably not all but most people who are working on this similar type of thing now, the coral larvae I show you, we're looking at the nervous system architecture. What type of neuron they have? Where are they located? What type of receptor sensors they have? Where they are present. We're hoping also to do the same neuronal markers of neural activity and see how they get affected by different conditions in the lab. How that affects larval recruitment and movement.

Then with the GWAS that Carly is going to do, again, go full circle, like I explained before, test genes, test different populations. The hope here is not just to do super spectacular images and results. Also if we identify those, we might identify that at a certain point. First, we need to identify how coral sense these recruitment queues. Once we do that, we can say, well, look, this coral from close to Florida, it works very poorly in cold weather, but then very poorly in warm weather, but this one from Panama actually doesn't care. It's great. Then we can use that information for screening populations and say, well, let's use this population for restoration or let's mix these two different populations to see what happens as a hybrid, for example. Eventually we can even see things that work better because once you know how it works, maybe we can create molecules that attract coral really well and then enhance recruitment even more or God forbid, if we go into that extreme in which we need to consider genetically modified animals for restoration, we can maybe make a coral that has a specific receptor that it's very good at recruitment, and then boom, we have a lot of coral growing very fast.

This is not something that we're going to do right away. If we go this way, obviously we'll work with ethics people with policymaking and make sure that it's safe and all of that. But at least it gives us the chance, and along the way all that information is invaluable for creating strategies and developing solutions. Many of us see this as there are incredible advances in biomedical sciences. We can try to treat different types of cancers or diabetes or whatever disease, but we can do that because of decades, if not centuries of seeing how the pancreas, the liver work, how neurons work. We know how they work normally, then we can go and see what to do when it goes wrong. For marine animals, we don't have that because we have very, very little information comparatively speaking.

One of our main initial goals is to provide that information, and then us and others can come with ideas that by definition, we cannot have them now because we don't know they exist. That brings us from this hardcore science into the other things that

we want to do. We are developing lots of initiatives, lots of programs, not just to do our research ourselves, but also to let other people enable them to do similar work. To put it in very simple In my opinion, one of the biggest problems we have is that we have, let's call them ecologists. They do amazing work in a coral reef or in a kill forest or whatever, but they really don't know much about cells.

Then we have a lot of very talented neuroscientists who know every little detail of every atom in a neuron, but they've never put their head underwater. We get things that have no mechanisms, and then we have lots of mechanisms that don't matter in the real world. What happens if we put them together, which is a little bit what is ADC nice. We are developing activities to train ecologists in cells and neurobiologists in marine biology. We have a special interest in developing countries and countries from other places in the world, in large part because I'm from South America, I'm from Argentina.

But also there are lots of species around the world that what we stickleback does not exist in the Southern Hemisphere. There are no tropical coral reefs in Antarctica. Can we get these tools and this idea of this pipeline into other places? As you all probably know, climate change is affecting developing countries more than it is affecting developed countries. Let's get that into the country, being able to do the science, too. We are organizing and organizing a variety of sessions in posterior congresses all throughout the world to push this field of neurobiology and changing environments, ecological neurobiology, however you want to call it.

Then for the inspiring the next generation of scientists, we have the best partner in the world, which is the Birch Aquarium. We've been working with Birch for, like, since I started here. Jeff told me, you have to it wasn't even an option. You have to work with Birch. I was like, great. then I was like, this is amazing, one of the best advices I ever have. This is one I've been showing. I really want to show this because I've been showing this presentation for about two years. We're going to do public lectures at the Birch Aquariums. Here we are.

I swear I didn't plan this, but I needed a selfie up. We're trying to get. I hope you agree with me that we have not just good science, but also visually appealing so we want to put that here and show that things are neurals are amazing, dynamic, colorful. Then the Changing Minds exhibit that Megan was referring to is coming in May, a year from now, basically. We're very, very excited to team up with Risa Puno, an interactive artist who takes place seriously. She was here recently for a two week stay. She talked with over 30 scientists from ADC9, eight different labs. Also went to USC, University of Southern California with 50 virtual aquarium staff members, guest educators, and she left us a message.

Risa Puno: [Music]

Martin Tresguerres: Some of Nathan Sinners fluorescent lines. Thank you. We are in constant communication with Risa through the virtual aquarium, and at the moment, I and Risa we're brainstorming what would be, and then the dream gets bigger and bigger, and I don't know what the final result is going to be, but it's going to be awesome.

Now, the thing about this model about neurobiology is that it is actually scalable to very, very broadly beyond neurobiology. These are some of the things now that I do in my lab. We're looking at lateral physiology of invasive muscles and other species. A person to Romberton who's here in the audience. Looking at biomineralization or how animals make their shells. This is a diatom, but also working with coral, sponges and others. Work from fatty, looking at photobiology and how that might allow corals to live in mesophoric environments, which is very deep, where there's very little light, but they're able to work there. It's very important because these places have been suggested as refuges for warming.

Then our fundamental information about how symbiosis happens when it is healthy is leading to ideas in which this is real data that we have a bleached coral, and then based on that information, we do our treatments, and now suddenly they're not bleach anymore, even though they are growing at five degrees higher. But what I want to convey here is that in addition to neurobiology, this is really applicable to pretty much every function that you might be interested in.

Then next steps, we really hope to go with this model and move from looking at our Forte, which is very, very awesome, but it's like small scale to how do we do that to simulate the environment as well as possible? Complex as possible, replicating natural viability, which is as if you imagine we cannot really follow a fish with glowing neurons in a Calforest with a microscope underwater. That goes us to think and brainstorm, which is one of the best things about this team is just like start thinking an idea. Half of the ideas are not good, but some of them are great. Specifically talking with Falko Coster, it's like, what if we can generate a virtual reality environment with many different conditions to simulate the natural environment in a lab, which is known as digital twins. This is already before ADC Falko working with Stuart and Sammy, they have these amazing representations of coral reef that you can go and look at every little hole in great detail.

As you can imagine, the conditions here might be different from there. What if we could simulate this in the lab while at the same time we change pH, we changed oxygen, we change temperature while we look at neural activity and then really see how these things work because in addition to the climate change aspect, I'm just fascinated about how animals can live in variable environments. Or what if we could even go one step further and take this digital twin that we may be doing half whole.

But then what if we go and do it in the field? It's one of my dreams is some of you might have heard about the RV Alpha Helix, which was something approaching from the NSF, from the 60s and 80s. They used to go throughout the world looking at the physiology and biology of different not only marine, but also terrestrial and doing work on the ship with biochemistry and other things that were available at the moment [Music] This was actually NSF funded by Run by Scripts. She's going to the Amazon,

Antarctica, Coral Ray, Grey Barrier Reef. This is recognize some of the landscape, looking at things such as like sub pressure in trees in the Amazon, coral reef, sole physiology of fishes, metabolism.

Then it ran for several years, then it went to the University of Alaska, and then I think it finished in Senada. But what if we could recreate something like that with new technology?

To finish up, it's like, this was one of these, cool to say it, but can we do it? More recently, I had the opportunity to go to Antarctica in this project with Alison and Bill. Again, while I was talking to Michael during this interview, I was like, I really like working in teams. That might be because I used to play basketball or some other things. I always teams here, teams there. This was a great thing that we went to Antarctica. Alison is a microbiologist. Bill is a chemist, I'm a biologist.

Now, let me translate that title for you. We're combining chemistry, microbiology, and ecohysiology to understand and use. There's this animal called a sea squirt that has a microbe. The microbe produces a compound, and the compound kills melanoma. They've been working on that for 15 years, and I got part of the team more recently. But going to Antarctica, looking at the sample and trying to do work in city was something that I wasn't sure how it was going to work out and it worked. It's great. This is very new. I just came back about four weeks ago, maybe five. Sekuliac ship of the University of Alaska. We were doing diving, ROV, drones, getting the animals, and then just being there makes you see how different the lab is from the real environment. One place from the other one, huge changes in CO_2, temperature. The animals are still there.

Then something that was very exciting and eye open for me that people of the team were doing what's called Oxford annopore sequencing. They were sequencing genomes overnight on a ship in Antarctica. We're doing microscopy. We're doing QPCR, which is analyzing gene expression in real time, and then based on the results we were getting, we would go and sample in one place or another. These are the sea squirts. Inside, they have these squiggly things that are called soil. They're animals, and they have the microbes, but we don't know where the microbes are. We don't know what it does for the symbiosis. That's part of what we're trying to do. These are images from reit in my lab, looking at the molecular basis of these symbiosis. I think that I have no doubt that these type of sophisticated experiments can be done, and I hope that they are done in the field. They're going to be pricey.

But this is where you have to define what prices. Is a couple of million dollars for the chance of literally saving biodiversity in the world. Is that expensive or is that cheap?

Just to finish up the Allen Family Philanthropy, they did a transformational investment. They gave us $10 million for four years. We are doing. We're almost halfway through, and I'm very pleasantly surprised of all the progress and all the opportunities. I'm also concerned and worried because 2028 is just very close to 2.5 years. Just finish our note. I cannot tell exactly how this information is going to help save or preserve biodiversity because I don't know what we're going to find, but I know that it will, the same way that knowing how cells work can help cure cancer by ideas that you don't know how they are, we are going to find that and we have a team that is special, is awesome. It's going to sound a little cheesy, but when I was living in Rio Gaseos and I was hoping to become a marine biologist, I didn't know how I was going to do it. I did it.

I didn't even know how you can look at cells working in real time, and somehow I found my way to do that, and that wasn't even really trying on purpose. Now that we have actually a goal to do it, I don't know how we're going to do it, but we're going to do it. The one thing that I do know is that to do that, we need, again, to have a team, and we need a much stronger, much bigger team. What we're trying to we're going to launch is this initiative called the a thousand by a thousand, trying to hope instead of relying on foundations and two years of writing a proposal, and maybe we get it or not, hoping to have like 1,000 people to donate $1,000 a year. That's $85 a month tax deductible. Using that money would give us $1 million a year, which is a good start to try to save the world. I would say it's a bargain.

Thanks. Thanks to the Virtual aquarium. Thanks to all of you for listening and yeah, I'll be here for any questions.

Thank you [Applause]

[Music]