Genome Insider Episode 7: Decoding Yellowstone's microbial mats

ALISON: Hey! I'm Alison Takemura, and this is Genome Insider, a podcast of the US Department of Energy Joint Genome Institute or JGI. Our intern and my fellow science communicator, Ashleigh Papp, is kicking off this story.

ASHLEIGH: So, billions of years ago, the world was a really different place. How then did our planet go from uninhabitable to a biological oasis, primed for life as we know it?

ALISON: The answer? Cyanobacteria!

DEVAKI: I thought about this, and then I think a nice way to say it is to put you into a time machine. And go backwards in time. So if you think about it human beings have been here about 200,000 years. So that's not the kind of time machine I'm talking about. I'm not talking about a 65 million years ago dinosaur time machine. I'm talking about two billion years ago. And that's when cyanobacteria were already hacking it. And that's pretty phenomenal.

Devaki Bhaya in the field, 2008. (Research Coordination Network)

ALISON: That's Devaki Bhaya, a plant biologist at the Carnegie Institution, at Stanford University. She studies cyanobacteria and how they interact with their environment and other microorganisms.

ASHLEIGH: These tiny little creatures, cyanobacteria, are photosynthetic. This means that they use sunlight to produce water and energy in the form of fixed carbon. They were the first organisms to produce oxygen, and we know that because of these fossils called stromatolites. These were formed by layers of cyanobacteria over 2 billion years ago.

ALISON: Without these little organisms, we probably wouldn't be here.

DEVAKI: It sounds very grandiose and it is because before that … the earth was anoxic. There was no oxygen. So these guys actually oxygenated the world.

ALISON: And it turns out we aren't the only lifeforms to benefit. A whole host of other organisms often live alongside cyanobacteria, taking advantage of the valuable resources that they provide.

DEVAKI: Bacteria don't live alone. And so, almost always they're in communities. And I think that's going to be the great new frontier that all of us are interested in is, how do communities work together.

ALISON: On today's show, we're talking to scientists who study cyanobacteria and look for clues in their genomes about how they're evolving and how they're interacting with other microorganisms.

ASHLEIGH: Devaki and her team are trying to understand how cyanos — as the researchers like to abbreviate cyanobacteria — are living in their microbial community. They want to know how they're changing on a genetic level, and, why?

ASHLEIGH: To study how cyanobacteria interact in their own little communities, Devaki and her team set out into the field to collect samples. They traveled to Yellowstone National Park, in the northwest corner of Wyoming. But, despite the park's beauty, I don't think they could've picked a more extreme environment to sample from!

DEVAKI: I was thinking, the first time we went to Yellowstone it was like walking into what has been described as what hell might look like. It's hot, it's sulfur, you know, it's dangerous. There's boiling mud. And I mean, it was unbelievable.

ALISON: They chose two different sites: Mushroom Spring, which is a flat, steaming pool surrounded by reddish brown dirt, and Octopus Spring, which lives up to its name … it has a big bulbous central pool surrounded by off-shoot pools that look like tentacles. Both springs are filled with freshwater that's heated by magma deep below the earth's surface.

ASHLEIGH: The average temperature of the water is hot to even hotter: from 60 to 90° Celsius, or 140 to 194° Fahrenheit.

ALISON: Oof, that's hot!

ASHLEIGH: So, the cyanos in these pools are known as extremophiles, or lovers of these extreme conditions.

The terraces of Mammoth Hot Springs are made of soft limestone and are constantly changing shape as water flows. Note: this area was not studied by Devaki and her team. (NPS / Neil Herbert)

ALISON: Because they're so hot, these pools are similar to life on earth some two billion years ago. And, in more recent years, both of these pools in Yellowstone have been well-studied by other scientists. So baseline information already existed, helping this project get oriented.

DEVAKI: For all of the audience who's listening to this, I would say: go there because there is nothing that compares with seeing that environment and how varied it is, how difficult the terrain is.

ALISON: But the cyanobacteria are not the easiest to get to.

MICHELLE: You have to hike in to actually go sample.

ASHLEIGH: That's Michelle Davison. She started working with Devaki in 2006 while getting her

PhD.

ALISON: Devaki and the research team wanted to sample the cyanos throughout the day to see how gene expression might be changing. And, one time, when Michelle was out at 2 AM ... well, she was fine, but ...

MICHELLE: I got a little lost on the way back. And I didn't have my bear spray. But everything worked out.

ASHLEIGH: And the springs that Michelle had to hike to? Are absolutely breathtaking.

MICHELLE: It's this beautiful bubbling cauldron of blue that eventually like fades to green as the temperatures cool down and the cyanos start to grow.

The bright, clear blue waters of Emerald Spring, in Yellowstone National Park, mix with yellow sulfur deposits to give off a bright green reflection. Note: this area was not studied by Devaki and her team, which cannot be shown in accordance with National Park Service policy. (NPS / Jacob W. Frank)

ALISON: The spring water itself is a light, clear blue, and the green around the edges of the spring are made up of the cyanobacteria. The cyanos live with and above other layers of organisms, and together they form what's called a “microbial mat.”

MICHELLE: So the mat is kind of like a rubbery texture. It's because these organisms create all these polysaccharides and create this matrix.

And when you take the samples you are taking a core borer, actually, and you're taking a sample of the mat, a plug of the mat. And it looks like one of those very fancy desserts that you would get in a high end restaurant, and you have all these layers and layers and at the very bottom, you have this charcoal gray layer, which is the sediment that's there. And then you have these layers of orange.

ALISON: These orange layers are dominated by two genera of bacteria, Roseiflexus and Chloroflexus. According to Michelle, these are cyanobacteria’s “lazy friends,” because they get all of their nutrients from the photosynthetic cyanos. All of these different organisms live together in a microbial community.

MICHELLE: And you can see that there's that community structure.... So it's a very appealing system to look at.

A slice of the mat core sample. The top green layer was used for metagenomic and single cell sampling. (Devaki Bhaya)

ASHLEIGH: You know, the sample that Michelle took of the microbial mats kind of reminds me

of a dessert that my Grammy used to make out of Jello. She would start off by making one flavor, and then layer in other flavors and colors on top of it … in the end, a piece, with all of its colorful layers, looked just like a rainbow!

But it's not Jello that we're talking about. These microbial mat samples are made up of living organisms and probably not nearly as tasty.

ALISON: Each microbial mat environment can be unique, and the nutrients that get exchanged within it also vary depending on who's there and what's available. But, in general, the cyanobacteria on the top use sunlight and carbon dioxide to produce oxygen and fixed carbon. The cyanos also fix nitrogen, pulling it out of the air to make it usable. Other members of the community harness these diverse nutrients.

ASHLEIGH: Another member in this microbial mat community are cyanophages. Phage means "to devour" in Greek, and these cyanophages prey on, or infect, cyanobacteria. We'll get to more on them a little later, but for now, you should know that they're a part of, if not necessarily invited to, the microbial mat party.

ALISON: Once Michelle and her colleagues had collected core samples of the mats, they packaged them up, kept them frozen with dry ice, and then shipped them to their lab at Stanford. In the lab, Michelle took some of the samples and began working on isolating and growing cyanobacteria. But she quickly realized that she had traded in the challenges of the field, for new ones at the bench.

MICHELLE: So one thing to remember is that these organisms that we're working with are just several generations out from the wild. They're basically — they're not model organisms. They've been taken from the mat. And we're culturing them in the lab. But they're still very much an unknown and a wild animal.

ASHLEIGH: This means that Michelle had to experiment with new tools and techniques. One example had to do with getting the wild cyanobacteria isolated.

MICHELLE: Because these cyanos are the primary producers of the community, getting them clean or away from heterotrophs that want to stick with them, and actually literally stick to them, can be difficult. So one of the tricks that we used was using phototaxis.

ASHLEIGH: Heterotrophs are microbes that, unlike the cyanobacteria, can't fix carbon to make food for themselves … and they try to mooch off the cyanobacteria. So, because cyanos are photosynthetic, Michelle realized she could separate the samples by using lights to attract the cyanos — kind of like a magnet attracting lead filings.

MICHELLE: And they would leave their friends or parasites behind and move towards light.

ALISON: Remember when we said that we would come back to the idea of cyanophages, or

viruses, in the microbial mats? Well, now is that moment. Michelle and Devaki are after all the genetic information that they can get about the microbial mat community. And now, that includes information about the viruses. But their investigation didn't start out this way.

ASHLEIGH: Viruses came into the picture, when the team's initial sequencing data turned up something called CRISPR.

ALISON: CRISPR, which is short for clustered regularly interspaced short palindromic repeats, is the bacteria's adaptive immune system. CRISPR is made up of short sequences from viruses that the bacteria have encountered in the past, so that, next time, they can recognize and neutralize these viruses. A remarkable feature of CRISPR is that the snippets of viral DNA are stored — like books in a bookshelf — in the order that they're encountered. They're like a historical record of infections.

ASHLEIGH: CRISPR was first discovered in E. coli in 1987, but it remained largely a mystery until the mid-2000s. It was around then that Devaki and Michelle found CRISPR arrays in the microbial mat bacteria. And at the time, the team didn't know the significance of the arrays or what to do with them.

DEVAKI: Believe it or not, we actually found these and we put them on the back burner because we didn't know what they were. And then the world exploded when the whole CRISPR story came out. We started looking into it and trying to figure out, well, this is telling us a story.

ASHLEIGH: The bacteria had wildly different numbers of viral snippets, called "spacers," which are nestled in between the CRISPR pieces. Here's Michelle:

MICHELLE: When we looked at the genomes ... there was an interesting contrast between the cyanobacteria and the Roseiflexus and Chloroflexus bacteria. They had CRISPR arrays that were very, very long like some of the longest, 700 to like 700 something spacers, where the cyanos had like, 100. So these two living side by side, it was clear that they had very different interactions with their phage even though they were living in the same environment.

ALISON: Devaki thought that the CRISPR virus sequences could lead them to clues about how cyanos and their predators interact.

DEVAKI: It's a little bit like a fishing hook, those little pieces allowed you to say, if I find this, I can kind of figure out who the partner virus is. So it quickly brought us into an arena that we were not experts in, which is to understand host and phage relationships.

ASHLEIGH: So, they decided to expand the scope of their experiment. Devaki and her team embarked on a journey diving deep into the interactions of the microbial mat community, viruses included.

DEVAKI: We will now, not just be able to do it just for cyanophage, but for the entire community,

get a sense of who the viruses are and how they are changing. This is kind of an arms race, right? The virus is changing, the host is trying to change. And we can try to understand that in a much more detailed way. Where does the virus tend to mutate, where can it not afford to mutate. And I think that would lead to a much deeper understanding.

ASHLEIGH: Because Devaki and Michelle wanted to learn about how the viruses and cyanos were interacting, they needed a lot of data. Normally, that would be a limiting factor. But JGI's Community Science Program helped to remove that barrier.

DEVAKI: So that Community Science Project allowed us to really expand the kind of data we wanted to collect. And what was fantastic about it was there was no limit to what we could ask for.

ALISON: Now, they're looking for genetic clues in a seemingly bottomless pool of data.

DEVAKI: Now we have the ability hopefully over the next three or four years to go into a lot of depth and use different data sets to ask questions. And I think, therefore, bring a lot more detail and more insights into what looks like a simple community, but it's far from simple.

ASHLEIGH: To try and understand what's happening on a genetic level in these complex communities, Devaki and her team asked JGI for three different types of data sets: metagenomes, single cell sequencing of microbes, and viral genomes. And the advances in sequencing technologies were almost too good to be true, resulting in way more data or "sequencing reads," than they expected.

DEVAKI: We had asked for, um, 50 million reads, something on that order for each sample. And when we got the sequencing back, Brian called me up and he said, you know there's something wrong here.

ALISON: She's referring to Brian Yu, who's a Research Scientist at the Chan Zuckerberg Biohub. He's on Devaki's team and was helping to process the sequence data sent by JGI. On the phone that day with Devaki, he said,

DEVAKI: We have 400 million reads. I'm sure they've done something, you know, they've mixed up our— something. It turned out not to be the case, because that's how many reads they get out of standard run now. So it was almost eight to 10-fold more than we asked for.

ALISON: So, Devaki, Michelle, and their colleagues began investigating the 400 million reads of data — generated from the Yellowstone microbial mat samples just so far. Currently, they have metagenomic data, a survey of the total DNA in the microbial mat. With all of that genetic information, Devaki and Michelle had to figure out how to organize everything.

DEVAKI: Once we got the data. I think it threw up a whole bunch of challenges. Some are which are, you know, really how do you work with such large databases. But the second question was,

how do we start to share data, and how do we as biologists start to really make sense of this.

The milky color of Porcelain Basin hot spring in Yellowstone National Park is due to siliceous sinter mineral deposits. Note: this area was not studied by Devaki and her team. (NPS / Jacob W. Frank)

ASHLEIGH: The researchers were sitting on what they called a treasure trove of data, thanks to JGI's Community Science Program. It turns out, there's another DOE resource out there to help.

DEVAKI: And it was a bit of serendipity. I was at the JGI annual meeting and there was an afternoon, and they said, you know you can join if you'd like to come listen to what KBase has to offer.

ASHLEIGH: KBase stands for Systems Biology Knowledgebase. It's a Department of Energy, Office of Science-funded organization. KBase is a cloud-based platform to help scientists analyze massive amounts of sequencing information, like the kind you would get from JGI.

ALISON: The KBase team worked with Devaki and Michelle to set up a 4-hour workshop to learn about their project and how KBase might help in the analysis of the massive amounts of sequence data that JGI had generated.

ELISHA: We went over for part of a day and worked fairly intensely with her lab, specifically on their data, just to understand what their data was, what kind of questions they had about their data, and what the ultimate sort of science question was in terms of how they wanted to look at the analyses.

ASHLEIGH: That's Elisha Wood-Charlson, the User Engagement Lead at KBase. She has a PhD in marine science and spent years studying microbes in marine environments. She's on the KBase team helping Devaki and Michelle to analyze their data from JGI. For the KBase team, it was fun to dive into the sequence data of microbial mats.

DYLAN: Devaki's system is fantastic. It's one of these settings that's perhaps representative of early earth conditions, right? And so that's why these hot Springs are so appealing as a system of study.

ALISON: That's Dylan Chivian. He's a microbial scientist and coding engineer at KBase. With Elisha, he's a part of the group that's providing resources and tools to help Devaki's team analyze the microbial mat data.

DYLAN: Her focus on the cyanos really gives us a glimpse into what those conditions might have been like for, you know, the chemical transformation of earth. So it's fascinating just from a pure investigation into nature itself.

ALISON: And not only that, but these cyanos are interesting from a biotechnological perspective,

DYLAN: Because of their ability to operate in these extreme conditions, thermophilic conditions and so on, they wind up having very interesting chemistries.

ALISON: To get into the mechanisms behind the chemistry of cyanobacteria in the microbial mats, Devaki and Michelle started with the metagenomic data from JGI, which had been organized, or binned. They tried out different ways of re-organizing the data to yield the most information possible, and eventually they got to assigning assembled genomes to certain organisms.

ASHLEIGH: KBase works like a lot of other cloud-based tools — you sign in with a username and password, and are taken to a dashboard page. You can start working on a new Narrative, which is like a step-by-step recipe that shows how you analyzed your data.

ALISON: You can think of KBase like a recipe book — you write down directions to make all of your favorite dishes, record the perfect times and temperatures, jot down the ingredient proportions that you've tested out, save different versions, and, then, when you're ready, share them.

ASHLEIGH: For Devaki and her team, the option to share all of their steps and information with other scientists is really helpful.

DEVAKI: We have collaborations that are across countries. So we have a group in the UK. And the question is, how do we all share this data in an effective way? And KBase, I think, allows that. That's one of the, what I see as a big advantage. It's like sharing your notebooks but with data — and big data.

ALISON: That kind of transparency can help accelerate fundamental discoveries, which is good, because as Dylan puts it, with this kind of sequencing...

DYLAN: We're talking about trying to understand the genetic potential of earth. And we just started scratching the surface of it.

ASHLEIGH: KBase is a platform that accelerates genomic analysis through crowdsourcing. And when researchers are ready to share their work, those analyses can be made available to everyone, in real time.

DYLAN: So that it doesn't take us, you know, a hundred years to start to have a picture of how the earth really works. It'd be nice to have that a little sooner.

Black Pool, in Yellowstone National Park, once contained cyanobacteria but now is too hot to maintain this life form. Note: this area was not studied by Devaki and her team. (NPS / Jacob W.

Frank)

ALISON: The pace of the coevolution, or the arms race, between cyanos and their phages is still a mystery. Now, the virus samples are being sequenced and the team eagerly awaits that data.

DEVAKI: The questions we ask can be much more reflective of the kind of things we care about.

ALISON: In addition to learning about cyanobacteria and their phages, the team is also hoping to explore how the system, the whole microbial community, is evolving.

ASHLEIGH: Fundamental research, like figuring out who's there and how they're adapting over time, can lead to unexpected discoveries that determine how these organisms could be harnessed in a lab or used as a model system. One example that the team discovered in phages were genes encoding lysozymes, an enzyme that the virus uses to hack through cyanobacteria cell walls.

MICHELLE: One thing that is really hard about cyanos is they are hard to break open. They are super hard to break open. ... a viral lysozyme that's been evolved in order to be able to lyse these types of cells, might be a very good tool that we could use in moving cyanos to be more of a model system, or in using them to create some sort of high value product.

ALISON: One example of a high value product? Biofuels. Because cyanobacteria fix carbon from sunlight, they produce carbohydrates and oily lipid molecules that could be used instead of fossil fuels. Breaking open their cell wall like a piñata would help release those goodies. Admittedly, Devaki may be a little biased, but she thinks cyanobacteria are kind of underappreciated by...

DEVAKI: …the Department of Energy. Cyanobacteria should be on their flagship, actually, because they do so much.

ASHLEIGH: Right now, Michelle is a scientist at the Pacific Northwest National Laboratory. She's translating what's been learned about microbial mat communities, to soil. Yep, it turns out that viruses are shaping the lives and genomes of microbes there too.

Understanding tiny little microscopic things, like viruses and microbes, helps us understand so much more about the world around us. But in a general sense, we know so little about viruses — like, how they work, or why they do the things they do. And the COVID-19 pandemic is yet another example of our lack of information. The outcome of Devaki and Michelle's work takes us one step closer to understanding more.

ALISON: For Devaki, harnessing the resources at JGI and high tech tools like KBase, is opening a future filled with potential for new discoveries about cyanobacteria and their communities.

DEVAKI: I'm just absolutely excited about what the next year or two is going to bring in terms of us putting together all of this information into insights that we really didn't have before.

ALISON: This episode was directed and produced by me, Alison Takemura and JGI intern Ashleigh Papp, with editorial and technical assistance from Massie Ballon and David Gilbert. Ashleigh was the lead writer on this episode.

ASHLEIGH: Genome Insider is a production of the Joint Genome Institute, a user facility of the US Department of Energy Office of Science. JGI is located at Lawrence Berkeley National Lab in beautiful Berkeley, California.

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ASHLEIGH: A shout out to the developers of KBase, a team that is spread across multiple labs including: Lawrence Berkeley, Argonne, Brookhaven, and Oak Ridge National Laboratories, as well as Cold Springs Harbor Laboratory, the University of Illinois at Urbana-Champaign, and the University of Tennessee.

ALISON: If you're interested in trying out KBase, they offer tutorials and webinars, for free! Check 'em out at: k-b-a-s-e dot u-s.

ASHLEIGH: If you enjoyed the podcast and want to help others find us, leave us a review on Apple Podcasts, Google Podcasts, or wherever you like to get your podcasts. If you have a question or want to give us feedback, Tweet us @JGI, or record a voice memo and email us at jgi dash comms at L-B-L.gov. That's jgi dash c-o-m-m-s at l-b-l dot g-o-v.

ALISON: And because we're a user facility, if you're interested in partnering with us, we want to hear from you! We have projects in genome sequencing, synthesis, transcriptomics, metabolomics, and natural products in plants, fungi, algae, and microorganisms. If you want to collaborate, let us know!

ASHLEIGH: Find out more at jgi.doe.gov forward slash user dash programs.

ALISON: And if you want to hear about cutting edge research in secondary metabolites, also known as natural products, then check out JGI's other podcast, Natural Prodcast. It's hosted by Dan Udwary and me. That's it for now. See ya next time!