

Controlling Your Microbes_ Michael Ibba

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SPEAKERS

Janet Box-Steffensmeier, Michael Ibba, Eva Dale, David Staley

E Eva Dale 00:00

From the heart of the Ohio State University on the Oval, this is Voices of Excellence from the College of Arts and Sciences, with your host, David Staley. Voices focuses on the innovative work being done by faculty and staff in the College of Arts and Sciences at The Ohio State University. From departments as wide ranging as art, astronomy, chemistry and biochemistry, physics, emergent materials, mathematics, and languages, among many others, the college always has something great happening. Join us to find out what's new now.

D David Staley 00:32

Mike Ibba is Professor and Chair of the Department of Microbiology and University Distinguished Scholar at The Ohio State University College of the Arts and Sciences. He serves as Associate Director of the Infectious Diseases Institute, and as Co-Director of the NIH funded Cellular, Molecular, and Biochemical sciences training program. Welcome to Voices, Dr. Ibba.

M Michael Ibba 00:55

Yeah, thank you for having me on.

D David Staley 00:56

I feel compelled to ask this first - so, could you first of all tell us a little bit about the discipline of microbiology, I assume that this is biology at a "micro" level, but maybe you can give me a better, more detailed definition?

M Michael Ibba 01:08

It's a discipline that started out with the idea that you were studying something you could only see with a microscope. So, you're studying the biology of organisms you can't see with the naked eye. Now that is no longer entirely true, there are some organisms that scientifically we think of as microbes that you can see with the naked eye, but I think a good generalization is to think of them as organisms you can't see with the naked eye.

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David Staley 01:33

Your research looks specifically at the mechanisms by which cells adapt and exploit new environments. Please tell us about this very interesting work.

M

Michael Ibba 01:42

Sure, so one of the things we're interested in is how cells adapt to microbes; in our case, we mostly look at bacteria, which is just one type of microbe. We're interested in understanding how they adapt to the various stresses and extremes of the environment that they encounter, whether this be temperature, a lack of oxygen, an abundance of oxygen, different environments. And we're interested in the molecular mechanisms by which they adapt, so how they switch their genes on and off under those conditions, how that changes phenotypes - that's, if you think about that changes the way they look and they act under different conditions, and they kind of program that genetically, and aside from our kind of scientific curiosity, what drives us in this is to understand how microbes can live and adapt in such a wide variety of environments. And the practical aspect for us, for example, is understanding how a microbe adapts inside you or me, whether it be in a beneficial way as part of a microbiome that helps you digest the food you eat and maintains your health, or whether it be an unwelcome microbe, which finds a way to live inside your body and possibly harm you despite your body's efforts to get rid of it.

D

David Staley 01:42

It seems like I've only recently heard or understood anything about our microbiome, and this seems to be sort of all the discussion now. How long have microbiologists sort of known about this, or is this really sort of new and cutting edge?

M

Michael Ibba 03:14

People have known about this as long as microbiology has existed, but I think that what the real change and the reason we're seeing it much more in the media and the public are more aware of it, is that it's in the last decade or a little over that, that we've been able to truly get our hands on the tools to understand how many microbes are part of our microbiome. So, a microbiome is simply defined as the big mixture of bugs that live with you on your body. And there have been lots of different ways of looking at this, but I think still one of the most useful is that you have at least as many microbial cells on an annual body as you do human cells, and they're very much part of what keeps you healthy and functional. And people have long been aware of the role of those microbes inside your intestine, inside your GI tract, how they help

you digest. One of the things which kind of brought this to the forefront was - this probably ages me but, I remember this notion that what gave you a stomach ulcer was stress. Now stress might -

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David Staley 04:26

It dates me as well, yes.

M

Michael Ibba 04:26

That might help you maintain your stomach ulcer, but the stomach ulcer was actually caused by a persistent microbial infection. And that awareness of how disruptions to the population of microbiomes in your body affects your health, the field has exploded beyond that. That's not something I work on, but, you know, in our department, we hire people, we have labs working in those areas, and it's really one of the growth industries of microbiology. And a great part of that is because there used to be such an overwhelming amount of complexity, but we didn't have a way to get a handle on it. But now, we have a means to collect all of the DNA from all the different microbes, all of that genetic complexity, and start to analyze it, and I think that's what's really changed the field is, before it was just an insurmountably large challenge to understand what was really there.

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David Staley 05:23

We say that there are new tools available, what are some of these tools? Is it an exaggeration to say that biology today is as much about data science?

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Michael Ibba 05:27

So, for example, to identify what all the different microbes are and how they change with your diet or with your genetics or with other things, you take a sample of them, you sequence them all. So when I say sequence them, you determine the sequence of their DNA, and the different species of microbes will all have unique DNA sequences that you associate with them. But then you end up with hundreds of millions, if not billions of pieces of data, and the first challenge has been to collect that data, and the next challenge is to analyze that data in a meaningful way so that you can see the biology for all the overwhelmingly huge data that's put in front of you. Oh, no, it's not an exaggeration, I think that's...it's become the thing that I think has empowered modern biology, is being able to come to terms with how much data is there and that we can now actually start to get a handle on it. And whether that be some of the groups in our department who really are about big data...this was a phrase I never really got my head around til I saw the size of the data sets, and... to give you an example, the first time my lab started doing this, someone, you get this work done, and someone simply send you a DVD with essentially hundreds of millions of variations of four different letters on it, and I don't have the skill set to analyze that, but the next generation of scientists that we train them our labs, do. And that's how you get your handle on, I think modern biology. That's just one of the tools, but it's a central tool, and I think that's what's driving us forward.

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David Staley 07:11

So you're looking specifically at microbiomes. I would guess, then, that the intestine or the GI tract is such a microbiome?

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Michael Ibba 07:18

Yes, I should say, I don't look at the microbiome, it's something that our field does a lot of. What I do is I look at how an individual component of the microbiome works. So we take a model organism, so these are organisms which have been very, very well characterized historically, and we have a lot of tools to work with, and so I try to understand how a single organism reacts to those kinds of conditions that they might encounter. But I don't study that yet, I mean, it's something we're starting to do, how those mechanisms play out when you've got everyone around you. So it's that kind of notion, I think, you can think about if you're trying to do something on your own in a field, that's one thing. If you suddenly got 100,000 people around you, you won't be able to do the same thing as you did when you're standing there on your own. But if you studied something standing on its own, you know what it's capable of, and then what it can actually do depends upon how everything else around it affects it. So I study the kind of... probably the slightly unrealistic individual standing in the field, and then, luckily for me, there are people in my department who study how that relates to the whole thing.

D

David Staley 08:32

So I know part of what you study are antibiotics, or at least how certain bugs are resistant to certain antibiotics. Tell us about this very interesting research.

M

Michael Ibba 08:41

So I think that the way that we come at this is - and I think, when I say we, I mean the field - is, we always used to wonder, I think, why antibiotic resistance would develop. And we tried to look for rationales as to, hoping that these were one off instances that we would be able to get around, but I think the way that the modern field - and I think this is very, very strong at a higher state, we look at so many different aspects of this - is most antibiotics, and I think people tend to forget this, are compounds that naturally occur in the environment. A lot of the antibiotics that are famous, so you know, penicillin, a lot of the antibiotics that came in the 50s, they are all natural products. So that means that they already exist in the environment, they might be made into derivatives that never existed naturally, but they're all generally based upon natural products. And in a kind of reductionist way, that means that resistance to those compounds already exists, because for organisms to thrive in their presence, resistance mechanisms have to exist. And so when you start to think about it like that, you see resistance as an inevitable event. What you're essentially doing is trying to, I know it doesn't sound very optimistic, avoid the inevitable. Now that can mean you delay the inevitable, I think this realization that resistance is on the way means that you can practice different stewardship with antibiotics, so use them more carefully. But I think understanding where they come from and how they work has changed because we think of them in a natural context, we don't think of them as these manmade miracle drugs. What man has been able to do is to make them in

quantities and make them available in ways that they can be very effective drugs, but you always have to remember that antibiotic resistance is an inevitable outcome to treatment with antibiotics, it's just about understanding when and how you will trigger that resistance.

D David Staley 08:41

So what's different now as we talk about antibiotic resistance, is it just that the day of reckoning is here or has something else happened?

M Michael Ibba 10:20

No, no. I would be more optimistic than that, I think that the day of reckoning is coming, but I think that the reason to be optimistic is that people understand where resistance comes from. People aren't throwing their hands in the air and wondering why suddenly resistance happens, it's understanding the mechanism by which resistance arises. I think this is where, rather than thinking of it purely as a pharmaceutical challenge, it's a, it's a challenge to understanding how you carefully use antibiotics in the clinic, how you are aware of possible outcomes and possible routes that might speed resistance arising. That's not something I do, but there's a very strong stewardship group at Ohio State who work around that very, very effectively.

D David Staley 11:41

Are we too careless with antibiotics in their use or their prescription? I'm putting you on the spot when I ask you that.

M Michael Ibba 11:48

No, no, I think it's a good question, because there's a strong media perception and it's a very easy out, especially if you're a scientist, to blame sloppy use by people other than yourself. But maybe we could say that, if we'd known better and even better informed the users, I doubt they would have ever administered antibiotics in a way that would have knowingly led to resistance. So, you can say that's poor scientific communication on the part of the scientists.

D David Staley 12:17

So to be clear, there's not an easy or even a difficult workaround to the resistance issue.

M Michael Ibba 12:22

Once you become aware of how resistance arises, you can develop new strategies, but they require time and effort and testing. I think it's important to bear in mind, we think about it as an antibiotic resistance crisis, but if you get an infection, you go into the medical center here, you'll be very grateful that they can find an antibiotic that will treat you and make you better. And that still is the case.

D David Staley 12:43

Yes. You're not saying we shouldn't be using antibiotics?

M Michael Ibba 12:47

No, not at all, I think quite the opposite. I think now that we understand antibiotics, I think that the usage is being much better controlled. And once you understand how they work, you realize that you need to constantly develop new antibiotics, I think you constantly need to, kind of, rotate the lineup, so to speak.

D David Staley 13:05

Well, since we're on the subject, I wonder if you'll tell us a bit more about the mission of the Infectious Diseases Institute?

M Michael Ibba 13:12

Sure. So, it's something I have to say I really enjoy being a part of. So one of the challenges you often have at Ohio State is that you have this huge potential benefit of scale that few other institutions can realize, but the challenge is to bring people together in a way that offers meaningful advances for them individually and for the institution. I'm not a big believer in building centers so that we can all pat ourselves on the back and say we built the center. I think our role, when we try to do these kinds of institutes is to constantly keep in mind that our members have got plenty on their plate already, and our goal is to try and offer them some different paths that they can't realize in their own colleges or departments, offer them the opportunity to interact with people that they may not be fully aware of at Ohio State, and to think broadly, as a result, to think broadly about these issues of infectious diseases. And I think that I've enjoyed it, because, you know, we might think about infectious diseases as you get infected with a drug resistant strain, and that's an infectious disease. But, you know, for example, Ohio State has huge strength in plant pathology, there's a big interest, of course in, in agricultural sciences and the vet school. There's a lot of different faces to infectious disease, but there are a lot of common interests and there's a lot of ability to realize synergies - this is another word which I found so overused for such a long time - but now actually seeing the potential for synergies where you bring people together and you can do things which are rewarding and different - that's, that's what we're trying to do. We're not trying to do much else other than that I would say, which to me is plenty to try and do.

D David Staley 15:04

What sort of disciplines are represented at the institute?

M Michael Ibba 15:06

Oh, so we have, I think we have something like 12 or 15, colleges, all of which I can't even remember. So, we have people from Public Health and Epidemiology, we have people from Nursing, the College of Medicine, Arts and Sciences, the Vet School, from the Ag colleges from, from all over, and people who bring very, very different perspectives. So for example, just if we look at the antibiotic resistance groups, me and several others work on the very basic science of the mechanisms. There are other basic scientists in the medical school who will look at how that might work at the molecular level during the infection in a host cell, then you have people in various colleges who then look at how you administer antibiotics and looking at the public health outcomes and looking at good and bad practices and improving stewardship, and the stewardship might be, it could be in the animal clinic or in the human clinic. So you see a lot of common interests manifested in very different environments, which I find fascinating to see and I'm so glad that we're finding ways to bring this together.

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David Staley 16:18

Does the Institute have any interaction with the CDC, the Center for Disease Control and Prevention?

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Michael Ibba 16:22

Yeah, so, there's... the antibiotic group have done quite a bit with them, they've worked with them, they've been given some contracts by them. So, and that's a good example of where the institute's helped to bring that kind of work to fruition.

J

Janet Box-Steffensmeier 16:35

I'm Janet Box-Steffensmeier, Interim Executive Dean and Vice Provost for the Ohio State University, College of Arts and Sciences. Did you know that 23 of our programs are nationally ranked as top 25 programs with more than ten of them in the top ten? That's why we say the College of Arts and Sciences is the intellectual and academic core of the Ohio State University. Learn more about the college at artsandsciences.osu.edu.

D

David Staley 17:00

Tell us a bit more about the Cellular, Molecular, and Biochemical sciences training program.

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Michael Ibba 17:05

So, yeah, one of my big interests, and you know, I think this is true of a lot of people in the sciences, is in graduate education, because one of the big strengths we have at Ohio State is we have incredibly strong graduate student groups. This is something that I co-direct with Karin Musier-Forsyth in the Department of Chemistry, and this is something that we put together. This is a program where we provide training in a variety of areas, all of which aren't immediately covered within the... so we have five member programs, and we draw students

from the different programs. And the idea here is that these are students who may have interest in pursuing different career outcomes, they may be looking for training in slightly different areas. So the goal of these programs is to, is to help train the future biomedical workforce. So we have a cohort of fellows, but what we've tried to do is to use the resources of this training program to kind of offer additional resources to our students in the life sciences in these different programs. So for example, based on student feedback, we've developed internship programs, we're now teaching a scientific writing class with Susan Lang, which is really a response to student demand. We've worked with other programs to kind of centralize responsible conduct of research and ethics training, which is a very big issue now in the life sciences. So, we've tried to utilize a kind of centralized effort to provide resources outwards into these programs. And we also use this as a recruiting resource because it's -

D David Staley 18:39
I'm sure.

M Michael Ibba 18:40
It's a way to bring strong students to Ohio State or even stronger students to Ohio State.

D David Staley 18:45
As a scientist, you must have a lab.

M Michael Ibba 18:47
I do.

D David Staley 18:47
Tell us about the organization of your lab.

M Michael Ibba 18:51
I generally have between five to seven graduate students - I have seven currently, because two of them are graduating within the next two months - two to three postdocs, I currently have two postdoctoral fellows in the lab. It's a very interdisciplinary lab, so currently, I've got to get this right, my graduate students I have some from microbiology, some from molecular genetics, some from biochemistry, some from the molecular, cellular and developmental biology program. We work quite broadly, so we have the five graduate students, these are PhD graduate students, two to three postdocs generally, and a variable number of undergrads, I would say, it's sort of seasonal. So, right now we have undergrads who are finishing up and

then more will come in the fall. So, and we also have some students that transfer from Columbus State because I help run a research transfer program there with the Postdoctoral Association.

D David Staley 19:45

Interesting. What sort of tasks or roles do the undergraduates play in your lab?

M Michael Ibba 19:49

We really try to tailor this around, around what they're looking for. So for some undergraduates, they'll be looking for, get a feeling for what undergraduate research is so that they can make a more informed decision about what they want to do going forward. Some come in with a more finished picture of what they want, some of those students will stay longer and develop more independent research projects. It really depends on the students, so the way we structure this is, all we ask is that the students, the undergraduates, work well, so to speak, with a postdoc or a graduate student, be respectful of their time. And then our goal, ultimately, is to help them become independent scientists by the end of their time. That's not what all students want, but we offer that for some students.

D David Staley 20:00

Yours sounds like a very interdisciplinary lab. Is that unusual?

M Michael Ibba 20:44

No, I don't think it is. I think it's the nature of science nowadays, at least in the life sciences. I don't know many labs which aren't interdisciplinary. I wouldn't get carried away, we do some biochemistry and microbiology, some genetics. It kind of speaks to how I was trained, and it's, I think it's very, very common.

D David Staley 21:05

Tell us what's next for your research.

M Michael Ibba 21:06

So one thing we've become fascinated, and my students might say I've become unhealthily interested in is... it's a phenomenon related to antibiotic resistance, which is challenging, it's very challenging, actually to study, which is, we know that during infections, a very, very small proportion of the bug that's infecting you will, to kind of simplify, it will go to sleep. So when you treat that infection with the antibiotic, because it's asleep, you can't kill it. So, you may clear most of the population of the bug away, but there's this danger that once you stop the treatment, and you think you're better, is that over time, those other cells can wake up.

D David Staley 21:56
It's like hibernation.

M Michael Ibba 21:58
Exactly, and it's called persistence. And so, we and a lot of other labs are fascinated by what triggers in this very small number of the cells this sort of dormancy, what makes them hibernate. And it's challenging, but it's fascinating at the same time, and so we've partnered with a group at Iowa State who are interested in the same topic and have some different expertise and, and we're kind of gingerly moving into this area. But, it's the classic example of high risk high payoff, and I don't hide that from the people on the project, but I've got some great people in my lab who want to roll their sleeves up and give it a shot, so.

D David Staley 22:38
What's the payoff, as you see it?

M Michael Ibba 22:41
I mentioned earlier about strategies to using existing antibiotics. It's a natural thing, is that normally when you use an antibiotic, you're targeting the majority, you can't take into account that very easily, that very, very small number that hibernate. And so I think what we're hoping is that once we know what triggers that, we can effectively treat both to truly clear an infection. If we know what triggers that small population, either we stop that trigger so that none of the population become dominant, the antibiotic will kill all of the cells, or we find a way to specifically also kill the hibernating cells.

D David Staley 23:21
Mike Ibba. Thank you.

M Michael Ibba 23:23
You're very welcome.

E Eva Dale 23:24
Voices is produced and recorded at The Ohio State University College of Arts and Sciences Technology Services Studio. Sound engineering by Paul Kotheimer, produced by Doug Dangler.

