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S1 00:04 From the Community Outreach and Engagement Core in the Center for Translational Environmental Health Research at Texas A&M University, we bring you the environmental health podcast. Our vision is to improve human environmental health by integrating advances in basic, biomedical and engineering research, and promoting translation of these advances between the bench, the beside, and the community. And now here's our host, Dr. Tim Lightfoot.

S2 00:32 Welcome to the podcast from Texas A&M's Center for Translational Environmental Health Research in the Community Outreach and Engagement Core, where we're striving to connect you to environmental health scientists, the people and passion behind environmental health, and how this work all affects you. I'm so glad you've that you've all taken the time to download us and you've joined us today. Joining us here in the studio today is another distinguished scholar that we have, Dr. Steve Kleeberger. Welcome to the podcast today, Steve.

S3 00:57 Thank you.

S2 00:57 It's great to have you here.

S3 00:58 Great to be here.

S2 01:00 Yeah. So Dr. Kleeberger is visiting us here at Texas A&M. I'm going to take a minute to tell the audience a little bit about you and why you're here, and then we'll just jump into our podcast conversation. Dr. Kleeberger is the principal investigator in the respiratory biology lab at the National Institute of Environmental Health Sciences in Durham, North Carolina. That's part of the National Institutes of Health. He has a PhD in Ecology and Environmental Physiology from Kent State University. He started out as a post-doc at Johns Hopkins and rose through the ranks there as a full professor. He was so successful in getting federal grant money, the federal government came to him and said, "Hey, we need to keep the money in-house. Come work with us." And so in 2001 he moved to the National Institutes of Environmental Health Sciences, as I said, where he served many roles including he's served two years as the Deputy Director of NIEHS, which is a big deal. He is a quite distinguished scientist. He's published over 160 peer reviewed scientific articles. He's got over 262 what we call citable items, a huge H factor of 44, almost 6,000 citations to date. Won a lot of awards, he's really a nice guy. He does a lot of work in respiratory virus work with the genetics of that. And so we're going to talk about that, we're going to talk about some other things as well, probably. So let's just get started. Here is Steve. Please jump in.

S3 02:21 Okay. Sounds good. Thank you for the introduction.

S2 02:22 You're more than welcome. You're worthy of much more than that [chuckles], but we only have 20 minutes. So it will probably take me about 35. So tell the audience a little bit-- a synopsis. If we were to meet you at a barbecue joint, which is-- we're in central Texas that's appropriate, and someone said, "Well, what do you do research on?" What would you tell them?

S3 02:38 So I'd tell them what we're interested in mostly is what factors contribute to differential responsivity or susceptibility to things that hurt the lungs. We're talking about air pollution, we're talking about respiratory syncytial virus, and we're talking

about other environmental factors that contribute to chronic lung disease.

S2 03:01 You said susceptible. Does this mean that it doesn't affect all people the same way?

S3 03:05 That's right. There's differential susceptibility to these environmental factors. Some kids and some adults get severe disease while others are mildly affected by the same stimulus or the same infection. And we believe that genetic background is an important contributor to that.

S2 03:25 But we really can't control it, it's just one of those things--

S3 03:28 You're born with it.

S2 03:28 It's something we're born with. So would knowing that help? Let's say I'm a parent and I have a kid and I know if they have a genetic predisposition to be susceptible. Would that help me prevent them from--?

S3 03:40 Hypothetically, sure. That's where the research is going, right? The idea is that this is part of individualized medicine, personalized medicine. And knowing a genetic predisposition or predisposing factor could, in many ways, guide a person's lifestyle that could guide how a person is treated for a disease. Cancer medicine is leading the way in that regard for personalized medicine for specific kinds of treatments that work in some people, but don't work in others. So we're just moving this into the environment health sciences arena.

S2 04:20 And this is not a new thing.

S3 04:21 It's not a new thing.

S2 04:22 Not a new thing. Been going on of a while.

S3 04:25 But the recent technology has helped a lot in terms of our understanding genetic factors that contribute to disease.

S2 04:34 I think the message so many times people get is that pollution is bad, but they don't get this it's differential for individuals.

S3 04:40 It's worse for some.

S2 04:42 Worse for some, not as much for others.

S3 04:44 Absolutely. And it's not just genetic. It's gender, it's age, its obesity, it's pre-existing diseases like asthma. They're a number of susceptibility factors or predisposing factors that contributes to susceptibility.

S2 05:03 Things you can control and things--

S3 05:04 And things you cannot.

S2 05:04 --you can't. I heard you do a great talk today on something called RSV. Tell the audience a little bit about what RSV is because we've actually done some of this translational stuff.

S3 05:16 Well that's right. Yeah with my good friend and collaborator in Argentina, Fernando Polack. RSV is respiratory syncytial virus and it affects primarily kids that are less than 5 years old and adults that are older than 65. It's a virus that infects everyone.

S2 05:36 So it's prevalent?

S3 05:38 It's very prevalent, yeah. And so by the age of 5 to 7, 90-95% of all people in the

United States have been infected with RSV, but only a certain population of them or a certain percentage of them actually get very severe disease. So the mild diseased people - that is kids and older adults - will present with upper airway symptoms, so they'll have nasal secretions, it's more like a cold. But with severe disease you get lower respiratory tract infection, and bronchiolitis, and you get shortness of breath, and wheezing, and they have to be admitted to the hospital. And so, there's a wide spectrum of diseases or phenotypes based on the same infectious disease. Globally, it's one of the most important diseases of infancy in terms of morbidity and mortality.

S2 06:35 Really?

S3 06:35 That's right.

S2 06:37 I mean, you presented some numbers on that. I was shocked--

S3 06:41 We're talking about millions of kids annually that are affected by this. And there is no vaccine. There was a trial in the '60s, I believe, with a vaccine that actually enhanced the disease and kids died from it.

S2 06:59 That's not a good outcome.

S3 07:00 That's not a good outcome [laughter].

S2 07:01 Not when you're doing a vaccine trial, no.

S3 07:04 But there are people all over the world feverishly trying to develop a vaccine, because of the major impact this disease has on especially kids.

S2 07:16 So how come people haven't heard about this? I could poll ten people, and none of them would say, "Yes, I've heard of that."

S3 07:24 The people that have heard of it are the ones who have had kids that have had it. And sometimes it's confused with influenza, but the mass knowledge about RSV, I agree with you, it's not there.

S2 07:44 You were telling us a little bit about some of your studies that you've done in Argentina, you mentioned it a few minutes ago, and that's after some extensive mouse work that you did because you establish a lot of stuff in mice first--

S3 07:56 That's right.

S2 07:56 --and to the basic physiology and then you transfer that into humans.

S3 07:59 That's right.

S2 08:00 If you can give our podcast audience a little bit of taste of what you did in Argentina with your collaborators.

S3 08:05 We've identified genes in our mouse and cell models that we found to be important in the response to RSV in these models. And we then asked whether the genes are also important in human populations. And so, we've identified risk alleles that has copies of the gene that people can inherit that may confer susceptibility to RSV infection, like we found with the mouse models and then with the cell models. We've been working with the Infant Foundation in Buenos Aires to recruit infants that have mild and sever disease with RSV infection, and ask whether the susceptibility variance in these genes that we've identified associate with the differential susceptibility or the mild versus severe disease. And we have come up with about half a dozen genes now that associate with increased risk for severe disease after RSV infection. We have a fantastic crew that work in these different hospitals throughout Buenos Aires and

they recruit the kids and we talk with the families and it's been a very rewarding experience to be able to translate what we find in our basic science models into real world situations.

S2 09:33 You have found some interesting stuff with socioeconomic strata of these children. Share that with the group and how that-- because it appears that socioeconomic status of the individuals actually affects their susceptibility.

S3 09:53 It really does, and what we're talking about is something called the hygiene hypothesis. And the hygiene hypothesis states simply that if you're exposed early in life to environmental stimuli that we believe prime the immune system to be better prepared to fight off consequences of infection, then you're going to be better off when you do get infected. And that hygiene hypothesis has been applied to asthma primarily, but what we have found recently is that the same hypothesis holds for RSV infection. So if you're predisposed or-- sorry. If you're pre-exposed to dog dander, endotoxin, cat dander, house dust mite, and all the things that you associate with being around lots of kids, lots of pets, it primes your immune system so that when you are subsequently infected with RSV, you can better fight off the disease. And the complication or the interesting twist that we put on this is that, hygiene hypothesis is also interacting with genetic background. And so, if you have a particular haplotype for important immunity genes, and the exposure, you can be affected adversely, or not, to the infection. So it's a hygiene hypothesis for RSV infection.

S2 11:28 So it's interaction? It's interaction--

S3 11:29 It's gene by environment interaction, exactly.

S2 11:33 That elusive thing is hard to measure.

S3 11:35 Exactly.

S2 11:36 Now you were telling me earlier that there's actually a company that has-- you have a patent-- you and your collaborator have a patent on some of these findings. And so there's actually been some effort to make this applicable, a tool that can be used.

S3 11:49 Well, we'd like to. That's sort of where we're heading with this. If we can come up with a diagnostic indicator of adverse outcome with infection to RSV, there are means to prevent the infection. There are means to attenuate the infection and by so doing, you reduce the health burden of the infection, but you can also potentially affect the adverse consequences after the infection, like asthma. And so we think that having a diagnostic tool to indicate susceptibility in kids and adults could have very important impact on public health, and other diseases like asthma and chronic bronchitis.

S2 12:36 So we want to make sure the audience didn't let that slip by when you said there maybe some interaction between RSV and asthma. Initiation of asthma.

S3 12:46 That's right.

S2 12:46 And that's a big concern? [crosstalk]--

S3 12:47 That's a very big concern.

S2 12:47 --large population has asthma.

S3 12:49 That's right.

S2 12:50 And so there are some hypotheses out there that says RSV may initiate asthma?

S3 12:55 I have been associated with-- severe RSV disease has been associated with asthma outcomes.

S2 13:03 That makes parents paying attention to RSV even more important.

S3 13:07 Exactly.

S2 13:08 Let's shift gears a little bit.

S3 13:10 Okay.

S2 13:11 We always ask our guests how they got into this. Did you like wake up one morning when you were like seven years old and say, "While I'm an adult I'm going to investigate RSV?"

S3 13:22 No. Didn't happen that way.

S2 13:27 So what is the path? Because we have people that listen to the podcast that are blossoming scientists themselves, and it helps them to understand the path that other people have taken.

S3 13:36 As you mentioned, I'm trained actually as an ecologist and evolutionary biologist.

S2 13:42 You did work with wolves, didn't you?

S3 13:44 And salamanders.

S2 13:45 And salamanders. Okay, that makes you qualified to do RSV.

S3 13:48 That's right. I think my post-doctoral fellowship is really what changed my research direction. And so I learned during my post-doc about environmental physiology. I met with a really bright other post-doc, Roy Lovett, who was doing genetics of asthma in mice. And I thought to myself, "What about air pollution and susceptibility to the adverse outcome after being exposed to air pollution?" And that got me started on the genetics again. And then I met Fernando, who was also a fellow at Hopkins at the time, and we started talking about RSV and the potential for genetic susceptibility, and it took us down that road. And so, sometimes it's just circumstances. Meeting the right people and interacting with them has been just a really thrilling part of being a scientist.

S2 14:54 Well that leads me to another question. Why do you do science? Science is not easy business. I know people think scientists have it made, but with the need to find grant money and to write publications and to continue that is always, "What have you done for me lately?" Not what you've done in the past. So why do you do science?

S3 15:14 Well right now we're doing it because of the translational aspect. And so what we're finding in the laboratory is directly translational to actually impacting on human health, and that's exciting. Everyday I come to work and I'm thinking, "What I'm doing today may have impact on future generations in terms of disease prevention," and so that's what drives you. And actually visiting in these hospitals with these kids who have the diseases, and talking with the parents of the kids that have the diseases and how grateful they are for the kind of work that we do - that is, you and me and the rest of us - that's what drives us. That's what is so interesting about what we do.

S2 15:57 Validation right there isn't it?

S3 15:59 It is validation. And it's also a motivator because you realize that what you're doing can have an impact on health.

S2 16:10 Yeah. Scientists are loathe to speculate but since we're here at this point and this is--

S3 16:17 You want me to speculate [chuckles]?

S2 16:18 I'm going to ask you to speculate, yeah. What do you see coming down the road? And we'll start with the bigger topic, the global topic of environmental health sciences. What do you think's coming and what are you going to be interested in to-- we know you're going to continue your work because you and I talked about it last night, you said you've got another 20 years of work at least. What are the big picture kind of things that people outside need to pay attention to?

S3 16:43 Well, I think we touched on some of those earlier. I think the personalized medicine. The potential to better impact populations that are affected by environmental factors in terms of disease prevention, but also in diagnostic capabilities. Again, to predict who's going to be susceptible to an environmental exposure, an environmental agent. Windows of susceptibility. So being exposed in utero, neonatally, as infants, even in childhood. So these different exposure times. These are really important factors that haven't been very thoroughly investigated, and I think that's where the future of science is going - at least in the environmental health sciences - Is to better understand these windows of vulnerability, predictors of adverse outcome and their interaction. I think really that's sort of the take-home that I would put forth.

S2 17:45 It gets more complicated and I know the public like simple answers. "Don't do this, don't do this. Do that." But sometimes it's, "Don't do this, maybe." Or "Do this, maybe." There's this study that's recently shown that not everybody benefits from exercise. A very small percentage of people. Don't take that as saying you shouldn't exercise. That wasn't the message there. But just some of--

S3 18:08 They don't have the same benefits that others do.

S2 18:10 That's right. There is some individual variation there. I think, as you said, that's almost a difficult message for the society to believe. It's like, "Why not me? Why didn't this apply to me?"

S3 18:22 And again, that gets back to the personalised and individual susceptibilities. Really important concepts.

S2 18:30 We sure appreciate your time today.

S3 18:32 Sure. It's been a pleasure.

S2 18:33 Coming in all the way from North Carolina to sit here with us.

S3 18:35 [laughter] It was a lot of fun.

S2 18:37 You visited a few other people, but [inaudible]. For full disclosure for those listening, I have known Dr. Kleeberger for many years.

S3 18:43 For years.

S2 18:46 We laugh a lot usually. Regular listeners of our broadcast will know this is the time we normally give our guest - all of our guests - the opportunity to give us a take-home message.

S3 18:55 A take-home message?

S2 18:57 What would you like people to remember from this podcast if they remember nothing else?

S3 19:01 I guess a take-home message is that no one responds the same way to the same stimulus in terms of environmental exposures. And understanding those factors that contribute to differential responsivity, inter-individual variation, whatever you want to call it, I think is really the key take-home message. That we need to understand what these factors are, and then once we understand them then they have to be implemented.

S2 19:28 Great take-home message. Thanks so much.

S3 19:30 You're welcome.

S2 19:32 And we want to thank all of you for taking the time to download and listen to us, and spend some time with us. We would hope that you would tune in in a couple of weeks when we put up another one of these podcasts. Continue to check back with us, because we'll always look for distinguished scientists that have a message and have a passion for what they're doing, and we want to share those folks with you. So until then, we hope that you remember that the environment does affect your health.

[music]

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