Dankesrede

von

Prof. Dr. Bonnie L. Bassler

anlässlich der Verleihung

des Paul Ehrlich- und Ludwig Darmstaedter- Preises

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Es gilt das gesprochene Wort!

Anrede,

I sincerely thank the Paul Ehrlich Foundation for awarding us this spectacular Prize. My thanks are on behalf of myself and my co-recipient Michael Silverman. Mike could not be here today due to health issues. Happily, Mike is on the mend. He is watching on the livestream. Hi Mike! Mike wants you to know he is sincerely grateful.

Mike and I are receiving our prize belatedly because of the tragic COVID crisis, but in a serendipitous stroke of good luck for us, we are awarded together with this year's winners, Doctors Karikó, Tureci, and Sahin who imagined, pioneered, and developed the COVID mRNA vaccine. Their work is awe inspiring. Your creativity and tenacity made it so I could be here today. Actually, your dedication made it so that all of humanity could be wherever each person is today. Congratulations to you and thank you.

I have been fortunate to receive a few prizes celebrating my team's research contributions. The Ehrlich Prize stands as the most significant because I am receiving it together with my former mentor Mike Silverman. I have dreamed so many times that this would happen. I thank the Ehrlich jury for making it so.

As you heard from Dr. Cossart, Mike and I wonder how bacteria get any bang for their buck. They are puny. They are primitive, Earth's first organisms, billions of years old. So seemingly simple. Yet, they have awesome power. Bacteria have traditionally been known for terrorizing us by causing disease. Now, increasingly, bacteria are known as our needed microbiome partners that supply us biomolecules that we do not have the capability to produce but are required for life.

Harmful or beneficial, how do bacteria achieve these grand feats? They talk. They count. They work as groups. Acting collectively allows bacteria to accomplish tasks that they could never carry out if they acted alone because, individually, each bacterial cell is too small to make a difference. We call this process quorum sensing, and we know it is the norm across the bacterial world. We also now understand that quorum sensing is essential for bacteria to be pathogens. Collective action is required for bacteria to successfully mount infections. Today, there are promising biomedical applications that interfere with quorum sensing and render virulent bacteria harmless. Hopefully, soon, these burgeoning applications will become medicines that

combat bacterial pathogens of global importance. Because compounds that disrupt bacterial communication target behavior, not growth, the notion is that these therapies will be less vulnerable to the development of resistance than traditional antibiotics. In this context, I find it especially inspiring that today's prize celebrates Paul Ehrlich and his contributions to immunology, his fight against infectious diseases, and his concept of selective "magic bullet" medicines.

In the 1970's, Woody Hastings showed that *Vibrio fischeri*, a bioluminescent marine bacterium, produced light only at high cell density. He discovered that the bacterium released and responded to the accumulation of a signal molecule, an autoinducer. Thus, *Vibrio fischeri* could sense when it was alone versus when it was in a community by tracking the buildup of the autoinducer. That finding went virtually unnoticed for a decade, presumably because the phenomenon, bioluminescence, was nothing more than a curiosity in an obscure bacterium.
And then Mike Silverman got on the scene. First, he had the realization that bacteria possessing the capacity to work as a group could be incredibly important. Second, and this is the genius, Mike realized that light production made the invisible bacterial word visible to him, the scientist. He could monitor light as a readout of bacterial collective behavior to discover the genes and proteins involved. In a series of six landmark papers published between 1983 and 1987, Mike Silverman, together with his unstoppable graduate student Joanne Engebrecht, discovered the *Vibrio fischeri* cell-cell communication components and their functions. Mike and Joanne cloned random bits of the *Vibrio fischeri* genome into *E. coli,* turned the lights off in the room, and looked for *E. coli* colonies on Petri plates that glowed in dark. That simple, elegant experiment yielded the enzyme that made the autoinducer, the autoinducer receptor, and the luciferase genes required for light production. The transferred system was sufficient to drive collective behavior. This breakthrough was the first molecular description of a quorum-sensing circuit. I looked at the genome database before coming to Germany. It reports 18,000 autoinducer-receptor quorum- sensing circuits, all of which possess genes nearly identical to those Mike and Joanne first revealed. All 18,000 of those discoveries, and many more that will come, can be traced directly to Silverman's original finding, the key discovery that revolutionized our understanding of bacteria and their profound importance in nature and medicine.

Okay, so I'm part of this story too! I was a beginning graduate student when Mike published those papers. I'd never read them nor heard of his findings. But, I was doing research on vibrio bacteria. Toward the end of my graduate training, I got to attend my first science meeting. I dutifully sat in the audience listening to the seminars. Mostly, I found them impenetrable: I

understood nothing. When I could comprehend the content, I found it, frankly, unremarkable and boring. I recall daydreaming about whether I even liked science. In the midst of these reflections, the next scientist got up to deliver his seminar. I imagine you can guess who it was. Mike Silverman laid out the experiment and discovery that I just related to you. I was mesmerized. The bacteria can work together? They act in synchrony? How could I, a microbiologist, not have heard of that? Tracking light production with only your eyeballs to assess collective behavior? What could be easier? Surely, I am smart enough to turn the lights off in the room and figure out which colonies glow and which are dark. I rushed to the podium immediately after Mike's talk and begged him to take me on as his postdoc. He... eventually... consented.

I arrived at Mike's lab in 1990 and no one was working on this project. No one. I asked him about that. I said, "Where is everyone" He said, "You are everyone". Lucky lucky me. My previous training was 100 percent in biochemistry. I knew no genetics nor molecular biology. I had never used a restriction enzyme. Mike taught me genetics and I fell in love with the discipline. We worked elbow to elbow for four years. Still focused exclusively on bioluminescent bacteria, together, Mike and I began to discover genes and proteins suggesting that quorum sensing might involve many proteins, sophisticated signaling mechanisms, and, importantly, more than one chemical "word".

Mike generously let me take my project to my independent job at Princeton University. On my last day in his lab he said, "I hope you put me out of business." That kindness launched my career. Another important point is that Princeton took a chance on me. Academia was not clamoring to hire me so they could capture the harmless bioluminescent bacterial research arena. No, the work was utterly fringe at that time. But, the Princeton Molecular Biology Department performs discovery science using model organisms. The possibility of chit-chat among the world's most ancient critters appealed.

28 years have now passed. I have my own group. And what a group. I'm standing here because of them -- adventurous, fearless, creative, tenacious, magnificent students and postdocs have joined this fray. We, together, made the ensuing discoveries. Early lab members took leaps of faith linking up with an untested assistant professor with a radical project. Now that the quorum-sensing field has become all the rage and is crowded with researchers, when lab members join, they still need to believe they can rise above the noise and make transformative findings. They do. We discovered that quorum sensing is not restricted to bioluminescent bacteria. Rather,

chemical communication among bacteria is universal. My team fleshed out the bacterial lexicon showing that bacteria use specific chemical “words” to detect self, related family members, non-related bacteria, and non-bacterial organisms. In every case, the chemical entities we discovered were brand new molecules to mankind. The group members showed how bacteria tailor their activities depending on whether they are surrounded by friend or foe. The team demonstrated that bacterial communication is essential for virulence in pathogens of global significance and that disrupting communication halts infection. In our most recent work, lab members discovered that bacterial communication transcends kingdom boundaries as viruses and higher organisms, including human hosts, participate in these chemical conversations. Our hope is that our research has provided a completely new way to think about microbes and, moreover, to combat them.

It is a privilege to live a life of discovery and Mike and I both know that. One’s days are filled with up-and-coming superstar scientists who want to transform the way we understand the world around us and find new ways to alleviate suffering. I always thought the best part of being a scientist would be me making discoveries. I was wrong. The best part is the people with whom I have shared the thrill of discovery—starting with Mike Silverman and now with the many trainees from my own lab. I thank Mike one more time today. Because of Mike, I also give the projects away when lab members leave. I understand I’m not losing anything: there are many lifetimes worth of discovery to make. Plus, having your former trainees eclipse you makes for the proudest moments. My former lab members are my meaningful legacy. I thank all the members of the Bassler lab, past and present, for your breathtaking accomplishments. I am so lucky to have you in my life. We did this together. This is our award.

Finally, there is one more adventurer in my mix. My husband, Todd Reichart. He is my biggest fan. Todd always tells me I can do it. He has been made an honorary member of the lab, but is never allowed to graduate. Todd, we did this together. This is our award. Thank you.

Mike Silverman also has a life partner, his wife Brenda who is also owed deep thanks. Mike and Brenda have been together since high school.

For Mike Silverman and for myself, once more, our heartfelt thanks to the Paul Ehrlich Foundation, to the selection jury, to our colleagues, and to our families. We are honored, overjoyed, and sincerely grateful for this prize.