Laudatio
von
Prof. Dr. Pascale Cossart

anlässlich der Verleihung
des Paul Ehrlich- und Ludwig Darmstaedter-Preises
2021

an
Prof. Dr. Bonnie L. Bassler
und Prof. Dr. Michael R. Silverman

Paulskirche, Frankfurt am Main
14. März 2022

Es gilt das gesprochene Wort!

Anrede,

The two microbiologists honored today by the Paul Ehrlich and Ludwig Darmstaedter Prize 2021, **Bonnie Bassler** and **Mike Silverman** have revolutionized our view of how bacteria behave in real life, providing an unexpected paradigm and a mechanism explaining why and how these microorganisms are, in many circumstances, so active and so important.

Bacteria are single cells – the smallest cells on earth – and had been, up to the work of the two laureates, considered as individual organisms living independently, feeding and growing independently and then dividing, one bacterium giving rise in general to two identical bacteria.

The work of **Mike Silverman and Bonnie Bassler** concerns all bacteria, these being pathogenic or not.

Indeed, for many of us, since the important work of Pasteur and Robert Koch at the end of the nineteenth century, bacteria are mostly considered as organisms responsible for a variety of more or less important diseases, such as cholera, pestis, tuberculosis and also sore-throat disease or gastroenteritis... However, as almost everyone knows now, in addition to the well described pathogenic bacteria, there are millions of non-pathogenic bacterial species which are present everywhere in the environment, in the soil, in the ocean, in the rivers as well as on plants and trees, on their roots and on their leaves. They are also present on and in animals and humans. They are present on their skin and also inside their bodies, in different locations such as the gastrointestinal tract, the oral cavity, the lungs etc.

In these locations, in contrast to the situation in laboratories, bacteria are not alone. They are surrounded by other microorganisms such as fungi and amoebas, and also viruses but they are the major constituents of these microbial assemblies and microbial ecosystems also called microbiomes. The most famous of these microbiomes is the intestinal microbiome because it has been first studied in great details but there is an increasing accumulation of new data concerning the ocean microbiomes, the plant microbiomes…**A new microbiology has emerged, and the two laureates' discoveries are at the heart of our understanding of the role and functions of these microbiomes.**

What **Silverman and Bassler** have shown is that **bacteria have a social life and sophisticated means of communication**. Indeed, in microbiomes, bacteria are not living and behaving

independently. They can communicate to their siblings or to closely related bacteria and they do so via chemicals. They produce the chemicals, they receive/recognize the chemicals and they respond to these chemicals by performing different types of tasks/activities. Within a given environment, all bacteria of one given category can receive the signals sent by bacteria of the same category and once the intensity of the signal reaches a certain level, and that all have received the signals, then they react in a similar way, acting as a group. They really only act as a group when all bacteria have received the signal, when the quorum is reached, one talks about **quorum sensing**.

How did **Bonnie Bassler and Mike Silverman** contribute to this breakthrough? And what type of actions do bacteria perform when they act as a group?

Mike Silverman – who later on became Bonnie Bassler's postdoc mentor – first took over the late Hastings' initial findings that some marine bacteria called *Vibrio fischeri* only produce light when they are in high number, that this can be reproduced by incubating bacteria in media from high density cultures and that the molecule in the culture media producing this effect is homoserine lactone, then called an autoinducer.

In the 1980s, **Mike Silverman** brought the power of genetics and molecular biology to this field. He succeeded to shot gun clone the *Vibrio fischeri* DNA into recombinant *Escherichia coli* to make a "glow in the dark *E. coli*". Remarkably, this strain produced the autoinducer and made light only at high density.

Silverman's subsequent cloning, sequencing, mapping, and characterization of the components encoded on the cloned DNA enabled him to discover the bacterial luciferase genes/proteins, the autoinducer synthase gene/protein, and the autoinducer receptor gene/protein. His elegant analysis of the role each gene played provided the world's first quorum-sensing circuit. Hundreds of similar circuits have since been identified, mainly when genome sequences became available. Scientists could only make sense of these genes by comparison to and reliance on Silverman's seminal findings. Silverman's achievements were accomplished long before the famous tool GFP – the green fluorescent protein – was discovered and used!

Bonnie Bassler took over Hastings' and Silverman's findings to an unprecedented level by showing that quorum sensing is not an exception but the rule in the bacterial world.

During and following her post-doctoral studies with Mike Silverman, she discovered that bacteria produce and use not one but multiple chemical signals to communicate and coordinate their behavior. She then showed that bacteria can communicate across species. She identified the universal interspecies communication signal called AI-2, a component which has a very peculiar structure with a very rare atom in biology, a boron atom.

In addition to light as shown for *Vibrio fischeri*, Bonnie Bassler showed and analyzed how quorum sensing controls biofilm formation. Biofilms are microbial assemblies formed on solid surfaces and surrounded by a kind of rigid structure which protects the bacteria from detergent or antibiotics. With the rise in antibiotic resistance, understanding biofilm formation, and disassembly is of critical importance paving the way for targeting quorum sensing, in antibiotic strategies.

Bonnie Bassler then showed that quorum sensing controls not only biofilm formation but also virulence in pathogenic bacteria. Many other scientists joined the field, working in a variety of systems and showing similar results. B. Bassler proposed that by manipulating quorum sensing, one can modulate virulence in important pathogens and showed that such a strategy was possible.

Bonnie Bassler also showed and elucidated how RNA-mediated regulation controls quorum sensing. She recently showed that bacteriophages which are viruses of bacteria could react to quorum sensing signals and respond via lysis or lysogeny.

Finally, it is worth noting that **Bonnie Bassler** is internationally recognized as an amazing and exceptional speaker. She explains simply and beautifully how bacteria talk to each other and act as groups. She has contributed immensely to the renaissance of microbiology.

Altogether, the two great scientists Mike Silverman and Bonnie Bassler have had a major contribution to the field of bacterial communication and social behavior. They are magnificent laureates of the Paul Ehrlich and Ludwig Darmstaedter Prize. Their achievements will guide many on-going and future studies on various microbial ecosystems.