Laudation for Dr. Tanmay Bharat[1]

Group Leader
Sir William Dunn School of Pathology, University of Oxford

Winner of the Eppendorf Award for Young European Investigators 2021

by Prof. Reinhard Jahn, Max-Planck-Institute for Biophysical Chemistry, Göttingen
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Even in the midst of the COVID pandemic, we should not forget that serious infectious diseases are not only caused by viruses but also by pathogenic bacteria. Indeed, I am certain that everyone attending the ceremony today has suffered from such bacterial infections, probably multiple times. Fortunately, due to the continuous development and refinement of antibiotics many of the major bacterial diseases can be effectively treated and thus have lost their threat. However, pathogenic strains are emerging that are resistant to all but the very "last reserve" antibiotics. Moreover, pathogenic bacteria have evolved additional strategies to escape the nasty antibiotics as well as the onslaught of immune system, some of which discovered only recently, and more research is urgently needed.

Today I would like to introduce you to one of such strategies that plays a much more important role than previously thought. I am talking about pathogenic bacteria that adhere to surfaces such as airway epithelia and others, where they form highly organized colonies. These colonies are embedded in an extracellular matrix produced by the bacteria, and they are termed biofilms. Indeed, persistent chronic bacterial infections usually involve biofilm colonies. In biofilms, bacteria exhibit "social" behaviour, i.e. they "know" about each other via various mechanisms of quorum sensing. Quorum sensing allows the bacteria to differentiate, in a kind of division of labor. Such colonies can be highly organized, with bacteria forming specialized populations with different metabolic activities and different rates of cell division. Particularly problematic is that some of the bacteria become metabolically

dormant, i.e. they persist for a long time and are largely resistant to all kinds of antibacterial treatment, but they can revert to active metabolism under appropriate conditions. Such infections can be extremely difficult to treat and may require surgical removal of the infected tissue as last resort.

The matrix of biofilms contains a mix of macromolecules that are produced by the bacteria and secreted into the extracellular space. They include polysaccharides, proteins, even DNA, and symbiotic viruses that are released and whose production is massively upregulated during the formation of such biofilms. These matrices surround the bacteria and frequently constitute the majority of the biomass of such colonies. Often they are structurally organized, for instance by forming tiny channels that allow for differential access to nutrients. Biofilm matrices form barriers for drugs by hindering their diffusion or by capturing them on poly-ionic surfaces on the matrix macromolecules in a kind of ion-exchange mechanism. Indeed, under adverse conditions the population-level survival of the bacteria is much better than of planctonically living species but the underlying molecular mechanisms are not well understood. Thus, we urgently need more fundamental research on biofilms, and this is exactly where Tanmay Bharat, the winner of this year's Eppendorf Young Investigator Award, has made seminal contributions. Before Tanmay tells you more about his work, I would like to briefly introduce him

Tanmay Bharat grew up in Delhi, India, where he completed his high school education. Already for his undergraduate training he moved to Oxford University in the UK, being supported by one of the highly prestigious Rhodes scholarships that is only given to the very top of international students. After completing his studies at Oxford University, he joined the laboratory of John Briggs at the EMBL in Heidelberg. It is indeed regrettable that we cannot have this ceremony at the EMBL, the place where Tanmay launched his truly remarkable career. During this time, the resolution revolution of cryo-electron microscopy had not yet started. Rather, cryo electron microscopy was considered as a kind of specialist discipline with important but limited potential for the future of molecular and cellular biology. At the beginning, Tanmay was involved in different projects. He has told me that for a brief time he worked on a project in my own field – on the SNARE proteins mediating neuronal exocytosis. Fortunately for me he did not continue because I would have gotten a very formidable competitor….Instead, Tanmay focused on the study of the structure and assembly of pathogenic viruses such as the deadly filoviruses (Ebola, Marburg), and retroviruses such as HIV. Without going into detail, the work was ground-breaking and led to several outstanding publications in top multidisciplinary journals.

For his postdoc, Tanmay returned to the UK where he joined the laboratory of Jan Löwe at the LMB in Cambridge. Here, he used and refined the novel high-resolution cryo-EM techniques to study the structure of macromolecules directly in their native environment, i.e. inside cells. Highlights from this time include the first atomic resolution structure of a bacterial surface layer, again leading to top-level publications. These successes have not gone unnoticed, and Tanmay has already won several prestigious awards including the EMBL Alumni Award and, most recently, the 2022 Colworth Medal of the Biochemical Society of the UK.

In 2017, Tanmay returned to Oxford where he became a group leader at the Sir William Dunn School of Pathology, and this year, he transferred to the Oxford Kavli Institute of Nanoscience Discovery. In his own laboratory, he decided to switch topics completely and to take advantage of his broad training for studying bacterial biofilms. (There was also a very strong personal motivation since he himself was affected by a persistent infection by biofilm forming pathogens). Already in a short time his lab has gained fundamental new insights, resulting in an impressive publication. However, I am not going to talk about this since Tanmay will tell you about his research himself. Let us welcome Tanmay Bharat, the winner of the 2021 Eppendorf Young Investigator Award!

[1]https://bharat.path.ox.ac.uk
[2]http://www.mpibpc.mpg.de/de

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