New approaches in the fight against bacteria

Infection biology at the Biozentrum is undergoing a paradigm shift: By shedding light on the interaction between pathogenic bacteria and their human hosts under natural conditions, researchers hope to generate novel ideas for treatment.

Research on bacteria and viruses has a long tradition at the Biozentrum. From the beginning, group leaders such as Professor Eduard Kellenberger and Professor Werner Arber made use of these microorganisms to study fundamental molecular biological processes. Their groundbreaking findings can still be found in textbooks today.

The last members of this “founding generation” were just about to retire when Professor Urs Jenal joined the Biozentrum a little over 25 years ago. “Microbiology at the Biozentrum had to reinvent itself,” he recalls. The new groups carved out their own approach, ultimately establishing the Biozentrum at the forefront of Swiss infection biology research.

“Over time, our work has increasingly been defined by a shared interest in antibiotics research,” says Professor Christoph Dehio, a group leader at the Biozentrum since the year 2000. This trend is explained by an alarming surge in bacteria that no longer respond well – if at all – to treatment with antibiotics. The WHO estimates that antibiotic-resistant pathogens are responsible for 700,000 deaths each year. These pathogens also increase the risk associated with routine operations such as appendectomies.

“We’re not just interested in understanding the underlying mechanisms – we want to find ways to successfully treat these infections,” explains Christoph Dehio. Efforts to this end resulted in the creation of the National Center of Competence in Research (NCCR) “AntiResist,” approved last year by the Swiss National Science Foundation and led by Christoph Dehio, Urs Jenal and Professor Dirk Bumann. Aside from the Biozentrum, the NCCR includes research teams of the University Hospital Basel and the ETH Department of Biosystems Science and Engineering (D-BSSE) at its primary location Basel, while additional research groups are based in Zurich, Lausanne and Israel.

Research under real-life conditions

“Until now, all antibiotics have essentially been discovered using the same approach,” says Christoph Dehio – specifically, by means of tests performed on bacteria grown in the lab under optimal conditions. Conditions inside the human body are quite different, however. “This is why we want to gain a better understanding of pathogens during the actual infection in patients.” Once researchers can reproduce these processes in the laboratory, the plan is for engineers to develop test systems mimicking patient tissue to screen for new active substances.

As an example of this approach, Christoph Dehio cites his own research on Escherichia coli, a gut bacterium that can cause acute and chronic bladder infections – and in severe cases can trigger life-threatening blood poisoning. To understand the mechanisms behind these infections, it is necessary to consider processes in the tissue of the ureter, bladder and kidneys, as well as the immune system.

“Solving the problem as a whole requires a transdisciplinary approach,” says Urs Jenal. “Such an approach depends on close collaboration between basic researchers, clinicians and engineers. With the NCCR we now have a framework that makes this possible.”

Jenal himself has a long-standing collaboration with clinicians at University Hospital Basel to investigate samples from cystic fibrosis patients. These patients generally suffer from chronic infections of their lungs with the bacterium Pseudomonas aeruginosa. “We want to understand how, over several decades, bacteria develop the ability to survive treatment with antibiotics virtually unscathed.”

– Prof. Urs Jenal

The two group leaders believe that in the medium term, the COVID-19 pandemic will result in greater awareness of the threat posed by antibiotic resistance. “The problem is not coming at us all that fast, but it is growing steadily,” says Christoph Dehio. Urs Jenal agrees: “The situation is going to get worse gradually, like a clock ticking.”

– Prof. Christoph Dehio