
POUR LE MERITE

REDE

EMMANUELLE CHARPENTIER
vor den Ordensmitgliedern und geladenen Gästen

am 2. Juni 2018
im Festsaal der Humboldt-Universität, Berlin

Sehr verehrte Ordenskanzlerin Nüsslein-Volhard,
Sehr verehrte Ordensmitglieder,
Meine Damen und Herren,

Ich freue mich sehr, dass ich mich heute Morgen auf dem historisch bedeutenden Charité-Humboldt Campus bei Ihnen vorstellen darf. Für mich persönlich ist dieser Ort ebenfalls von großer Bedeutung: Hier nahm die moderne deutsche Mikrobiologie ihren Anfang und hier darf ich mein eigenes Max-Planck-Institut für die Wissenschaft der Pathogene aufbauen.

Please allow me to switch to English now. Although I learned German at school and further made some efforts to master your language during my time in Vienna, Austria about a decade ago, my level in German does not currently permit me to deliver to you my speech of today in your language. The future will be better! The future is always better…

I am very honored and humbled that you have decided to elect me as a member of the Orden Pour Le Mérite and join your prestigious circle of personalities in arts and sciences, an, I would like to quote in German "illustrer Zirkel menschenfreundlicher Heiterkeit, die Heinrich von Treitschke noch als eigentümlich für den gebildeten Deutschen ansah" . The quote is taken from a detailed article about Pour Le Mérite and its members in Die ZEIT, back in 1976, in which the journalist Nina Grunenberg praised the noble minds of the circle. Four decades have passed, but I am convinced that the spirit of its members has not changed, and I am looking forward to getting to know you and your great minds. In the meantime, I would like to take this unique opportunity to speak to you and tell you a few words about myself.

Your decision, to elect me into your circle is largely based on my work about the transformative CRISPR-Cas9 gene editing technology – a discovery that is considered by

the scientific community as "a revolutionary breakthrough" or "a game changer in the field of life sciences" (I will come to that later in more detail), I am often asked if I had always been interested in becoming a scientist – and the answers is… probably yes.

Obviously, this was not that clear to me during my time at middle school. But at a young age, I was already very determined to continue as far as possible with my studies, go to University and acquire more knowledge in sciences. I did not have any special field in mind back then, I was interested in natural sciences as much as in mathematics or the humanities (philosophy, sociology, psychology).

Nevertheless, I recall a conversation between me and my mother in the nineties which reveals that my desire to pursue a career in science started in fact early. While I was a student at the University Pierre and Marie Curie in Paris, I informed my mother that I had chosen my host laboratory for my Master thesis at the Pasteur Institute. She then recounted that, at the age of 12, I came back from school one day and let her know that I will be working at the Pasteur Institute. I suppose that a subject of study at my biology class must have triggered this wish. But this short conversation still makes me think how much of my path was already laid out very early on.

My real desire to become a scientist did not start before the later stages of my studies in microbiology. My projects during my Master's and PhD thesis combined medical microbiology and the genetics of traits such as of antibiotic resistance. I felt a strong attraction to this field, not only because of its importance given the fast emergence of antibiotic resistance at the time, but also because I simply enjoyed the process of experimentation, from planning to execution and analysis. I felt at home in the lab. Already during my Master's thesis, I was given a lot of independence and responsibility for my projects. Looking back, I think this had a very positive influence on my career, because I identified myself very early on as a scientist rather than a student – as someone creating knowledge rather than simply absorbing it.

I did not start working on the CRISPR-Cas9 system until many years later, but it was clear to me by the end of the 1990s that I wanted to make microbiology my profession. This meant that I needed to leave France and reach out to other countries and research cultures, the United States at first and then Austria, Sweden and Germany. Since then, mobility has become a recurring theme in my life which, I strongly believe, has made me the scientist I am today.

When I moved to the United states, I was used to a more conservative European research tradition and found it highly motivating that my colleagues across the Atlantic were enthusiastic about their work in a way that they did not mind taking risks or failing with their experiments. Back in Europe, in Austria and Sweden, I was fascinated by the international atmosphere in the labs and the support for young aspiring scientists. I enjoyed freedom and trust in my work, although I did not have much to show at the time.

I had a very clear motivation for each move - there was either a specific topic I wanted to study, new scientific strategies and approaches I wanted to learn, or new colleagues I

wanted to work with. Nevertheless, I was always confronted with unexpected and new challenges that come with moving to a new country and working in new environments. Mastering these challenges has always been a very enriching experience and made me a better scientist.

CRISPR came into my focus in the beginning of the 2000's when the system was described as a molecular signature to further type clones of bacterial isolates. In Vienna, in 2006, my lab performed a bioinformatics screen to search for new molecules of small RNA nature in the human pathogen Streptococcus pyogenes and identified the tracrRNA and CRISPR RNAs of the CRISPR-Cas9 system. At that time, CRISPR was hypothesized to act as an adaptive immune system in bacteria and archaea that would involve RNA-guided proteins to target the genomes of invaders, for example viruses or plasmids. In 2006, this hypothesis still needed to be tested and nothing was known about the mechanisms that would then be involved in such immunity.

I saw this fundamental topic of microbiology as an opportunity to discover new types of RNA interference mechanisms. It was also clear at the time that CRISPR had largely evolved in multiple sub-systems in procaryotes and a large number of diverse mechanisms would be expected to be discovered, some of which could be harnessed to target genomes and their expression for biotechnological and biomedical purposes.

Our seminal paper describing how the CRISPR-Cas9 protein, CRISPR RNA and tracrRNA components work together in the cell appeared in Nature in 2011. One year later, my collaborators and I published in Science how the three components could target foreign DNA: Here we also showed how the system can be harnessed as a powerful tool to target and edit specific DNA sequences in a very precise manner.

Since then, the CRISPR-Cas9 technology has transformed the world of life sciences and my life along with it. I am overwhelmed by the number of scientists and laboratories around the world that are further developing the technology into innovative applications in biotechnology, agriculture and medicine. CRISPR-Cas9 has triggered high hopes especially for the development of therapies against serious genetic diseases, for which there are currently no treatments available, but also against cancer and HIV to name only a few.

But there is also the other side of the coin: A powerful technology such as CRISPR-Cas9 also bears certain risks, especially when it comes to modifications in the human germline. Despite the fact that our discovery is still very young and we are far from understanding its implications, we can already see that private interest and the desire for human enhancement advance unethical applications in regions of the world without strong regulations. I personally find these deviations not acceptable and I am happy that scientists including myself strongly call for an international debate and revision of international laws in this regard.

We are currently experiencing a "CRISPR craze". So, many people outside science are often surprised when they learn that our discovery is a result of basic science. Being a microbiologist, I sometimes see my field of research overlooked or not given the public

attention and funding it deserves. But, the CRISPR-Cas9 discovery is a very good example why basic science is fundamentally important. Without the deep understanding of its basic mechanisms, we would not have been able to develop it into the innovative technology it is today.

When I talk to young scientists these days, many tell me that they envision a life outside research, a secure position in the industry. Maybe the noncommittal nature of today's society results in a stronger desire for fixed frames. Personally, I find this development very disappointing. I would like to encourage young talents to engage more in fundamental research, to look deeper, to take risks, to follow their instincts, although the path may be stony. Yes, basic science is arduous work, and often it takes years until results are visible. It requires a lot of patience, dedication and commitment. It is not an easy profession. And funding is hard to secure.

To change this, we need to advocate for and to be aware of the achievements and enormous potential of this field. Tools and methods that have revolutionised the life sciences would not have been possible without fundamental research in microbiology. And yet, there is a treasure trove of mechanisms and new tools to be discovered in the microbial world. Research on the basic biology of microbes has also led to many effective treatments against infectious diseases which pose a great risk to human health and the economy, as recently highlighted by a high-level meeting of the United Nations. It is our responsibility as microbiologists to lead the way in developing novel and durable strategies to combat infectious diseases.

The world needs a new generation of gifted, curious and passionate scientists to tackle the many questions that are still untouched, and I am determined to support them with all my heart.

Thank you.