

I CAME INTO MY OWN IN THE MICROWORLD

He works in the Protein Engineering ICRC research team at the Loschmidt Laboratories, Faculty of Science, MU. In 2020, he was awarded a Fulbright Scholarship to spend a semester at the University of Texas at Austin in the group of Prof. Kenneth A. Johnson. This year he successfully defended his PhD in Molecular and Cell Biology and Genetics. For his thesis on “Rational protein design guided by kinetic studies” he received the MU Rector’s Award. He repeated his success from 2018, when he was awarded the same prize for outstanding results in his Master’s studies. In the interview, he describes his scientific beginnings and his successes in researching “glowing” enzymes or stroke drugs.

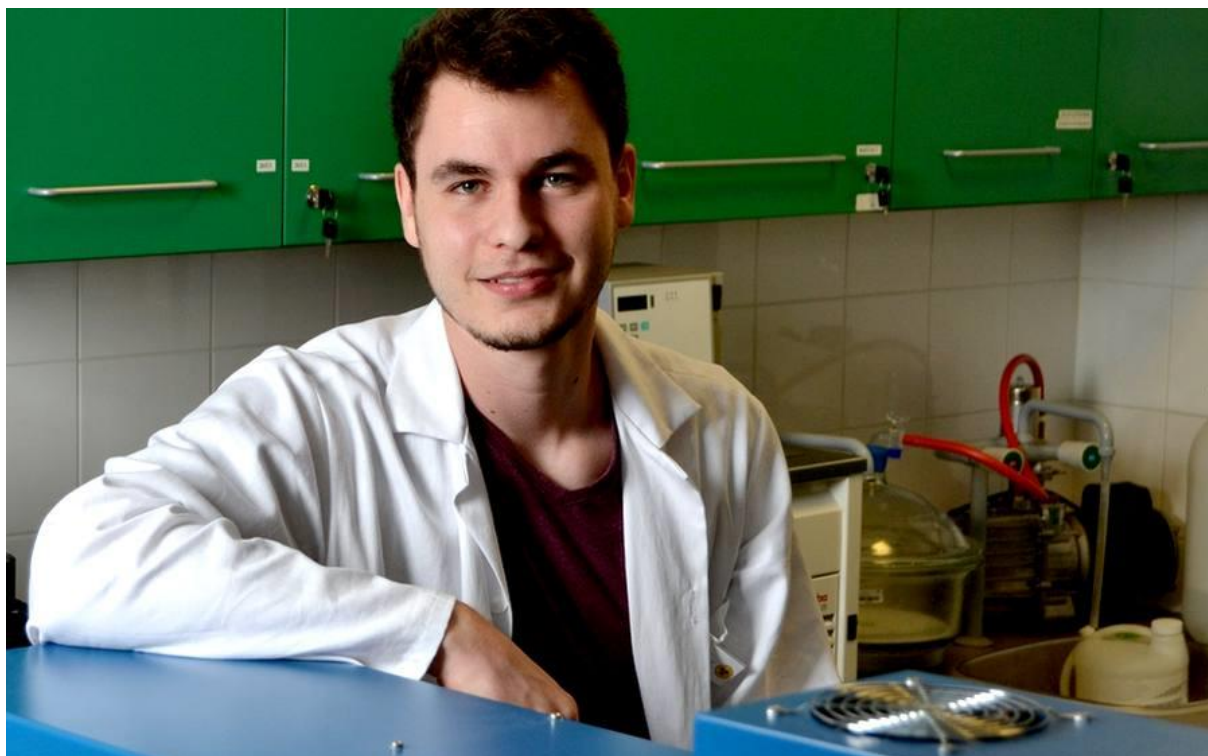


Photo: RNDr. Martin Toul, Ph.D.

What was your path to science?

I think that every young child has a kind of scientific or exploratory spirit in him, as he/she discovers the world around little by little. Not every such spirit, however, survives into adulthood. For me, this interest persisted, which is actually the reason why I took the path of science. Thanks to my older sister and her school notes, I was interested in chemistry from about the second grade of elementary school – I loved learning the names of chemical elements, filling in their names in crossword puzzles, and looked forward to taking this subject in school as well. Although I also enjoyed math and physics, chemistry always led the way. So, when choosing a college, my direction was quite clear. Interestingly, perhaps, I never had a very positive relationship with biology and only got more in depth with it by choosing the Biochemistry program, as I saw more potential in connecting chemical research with living nature. In the end, it turned out that while the areas of animal and plant biology discussed in elementary and high school were never really likely to excite me much, the microworld at the level of biomolecules, DNA and proteins, was where I came into my own. Thus, my current research combines biology with chemistry, as well as physics and mathematics, so I am doing exactly what fulfills me the most.

What exactly are you researching?

In our research group at Loschmidt Laboratories, we are generally involved in protein engineering. This means that we specifically modify a protein to exhibit improved properties or to get rid of unwanted side effects for more effective use in practice. In fact, proteins find a variety of applications, whether as drugs in clinical practice, components in diagnostic kits, or reagents for the production of important materials in biotechnology. Thanks to protein engineering, we can improve the efficiency of these molecules, their heat resistance, or even the selectivity of a given process, to make their use in practice and industry real. I am specifically focusing on, among others, two important groups of proteins. The first group is thrombolytics, used as drugs to dissolve blood clots in stroke or myocardial infarction. The second group are luciferases, bioluminescent “glowing” enzymes that are used in diagnostic kits but could also serve as an alternative source of glow in the future. However, all of these proteins suffer from certain weaknesses that need to be addressed for them to perform their role truly effectively for their intended purpose. And that is what protein engineering modifications are designed to do.

What was your PhD thesis about?

My PhD thesis focused on the use of advanced kinetic methods to reveal the major weaknesses of the proteins studied and their subsequent removal. The biggest stumbling block in protein engineering is that, in the case of imperfect proteins, we don't initially know exactly what needs to be changed and improved about them to make them more effective for a given purpose. And it is detailed kinetic analysis that is one of the tools to uncover the precise mechanism of how proteins work at the molecular level, and also to identify which step of this mechanism is the so-called limiting step. This allows us to specifically target this major weakness and make targeted adjustments, greatly increasing the chances of successfully improving the protein rather than if we were to randomly adjust it “blindly”. By this strategy, we have been able to create, for example, a modified thrombolytic with the potential to exhibit a reduced risk of bleeding after administration, or an improved luciferase with a 100-fold increase in luminescence for long-term emission of bioluminescent light.

How would you explain the benefits of your research to a non-scientific audience?

In the thrombolytic protein project mentioned above, we want to improve the current stroke drug and develop something more effective that could save many patients around the world. Nearly 18 million people die from cardiovascular disease (largely myocardial infarction and stroke) every year, which is a terrifying number, so the motivation is huge. As for research into the luminous enzyme luciferase, there are several possibilities. In diagnostic practice, luciferases are widely used to detect various biomarkers (i.e. measurable indicators) of disease, so improving them will allow us to make this detection even more efficient and sensitive, or to extend it to capture other important substances. Outside of clinical practice, there is then huge potential to use luciferases as an alternative light source to conventional lamps. With a system based on biomolecules, such illumination could be fully renewable and sustainable.

Did your time at the ICRC contribute to your success?

Definitely. The connection of our research group to the ICRC was crucial. It has given us access to clinically oriented projects that are very attractive and bring a specific application potential to our lives. At the same time, thanks to the ICRC, we were able to create a large consortium STROKE Brno, which brings together experts from many fields. This takes our stroke research to a much higher level and allows us not to stop researching only at the level of a scientific paper, but to try to take a possible new drug to the next stages of testing. As part of the collaboration, it can be tested on real human blood clots and also in vivo in animal models to see if it is indeed an attractive candidate before possible clinical testing. As a result of the connection to the doctors at FNUSA,

we are also assured that the research is moving in the right direction and that we are not trying to improve something in laboratory conditions that no doctor will use in practice anyway.

What are your future plans?

I have just finished my PhD, so I am looking forward to moving into new and interesting scientific areas to broaden my horizons and learn something new. I am now heading for a postdoctoral position abroad. I went through several interviews and finally decided on a position at the Belgian VIB institute, which will fulfil my future plans in the next few years. Subsequently, my current vision is that I would like to return to the Czech Republic and do my own research in academia here. However, I am open to different opportunities, so maybe it will turn out differently and I will end up in another country or a biotech company. Who knows?! In any case, I would like to stay in a scientific environment and continue to explore the unexplored.

Thank you for the interview and I wish you continued success in your research.

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