ZAGADNIENIA
NAUKOZNAWSTWA
2 (220) 2019
PL ISSN 0044 – 1619

Prof. Marcin Drąg – FNP Prize Laureate 2019

DOI: http://dx.doi.org/10.12775/ZN.2019.019

Prof. Marcin Drąg from the Faculty of Chemistry at the Wrocław University of Science and Technology has received the 2019 Foundation for Polish Science Prize in the field of chemical and material sciences for developing a new technological platform for obtaining biologically active compounds, in particular proteolytic enzymes inhibitors.

Marcin Drąg was born in 1975 in Świdnica. In 1999 he completed his Master's degree in Chemistry at the University of Wrocław. He earned his doctorate at the Wrocław University of Science and Technology in 2003, and his postdoctoral (habilitation) degree at the same institution in 2011. He was nominated as full professor by the President of the Republic of Poland in 2016 at the age of 41.

He has worked at the Faculty of Chemistry at the Wrocław University of Science and Technology since the start of his scientific career. He is also affiliated with the Sanford Burnham Prebys Medical Discovery Institute in California, where he holds an Adjunct Professor position. In addition, he completed research fellowships in esteemed institutes, including the École Nationale Supérieure de Chimie de Montpellier in France, Technische Universität Wien in Austria, and Emory University in Atlanta, USA, among other institutions.

He is a laureate of the START, FOCUS and TEAM programmes of the Foundation for Polish Science, and several times laureate of the OPUS and HARMONIA programmes of the National Science Centre (NCN) in Poland. He has also been recognized multiple times with the Rector's Prize of the Wrocław University of Science and Technology and the Prize of the Minister of Science and Higher Education. He was awarded in WROCŁAW'S 30 CREATIVES programme in category "Science" by Wrocław City Council in 2018.

He is a co-inventor in/of nine patents and has published nearly 110 scientific papers in leading journals, including *Proceedings of the National Academy of Sciences*, *Nature Reviews Drug Discovery*, *Nature Communications*, *Nature Protocols*, *Nature Chemical Biology*, *Journal of the American Chemical Society* and *Chemical Science*, among others. His work has been cited over 2,000 times, giving prof. Drąg a Hirsch index of 28.

The 2019 Foundation for Polish Science Prize recognizes prof. Marcin Drąg's achievements involving a new technological platform which uses a wide range of

unnatural amino acids for developing chemical tools for monitoring the activity of proteolytic enzymes. This platform may be used to develop new therapies, drugs, and diagnostic methods.

Proteolytic enzymes, also known as proteases, break down proteins into smaller fragments: peptides and amino acids. Thus, they play a key role in both health and disease. Proteases are fundamental to numerous processes such as embryonic development, blood clotting, cell death, and the development of immunity. However, the dysregulation of their activity is linked with plethora of diseases such as cancers, diabetes, neurodegenerative disorders, but also viral and bacterial infections.

Given this, proteases play a huge/immense role in biomedical research. Prof. Marcin Drąg's research specifically involves the design and synthesis of small-molecule activity-based probes and inhibitors, biologically active compounds, which can be used for the selective monitoring and/or blocking of the activity of proteases.

The technology developed by prof. Drąg in called HyCoSuL, Hybrid Combinatorial Substrate Library. This method utilizes a large panel of unnatural amino acids that can deeply explore the chemical space in proteases active site, yielding selective peptides that can be further transferred into fluorescent substrates, inhibitors or activity-based probes (ABPs). By combining chemistry, biochemistry and molecular biology, prof. Drąg and his co-workers, created a cutting-edge research platform to examine numerous medically significant enzymes.

In his pioneering work, prof. Drąg used HyCoSuL technology to develop chemical marker (activity-based probe) for neutrophil elastase, a serine protease which plays an important role in the development of cancers and also participating in the process of pathogen killing. This molecule, which is several thousand times more active than others available on the market, can be used for selective identification of this protease in neutrophils – the most abundant type of white blood cells. In a follow-up study, prof. Drąg's team designed a set of fluorescent markers that were used for simultaneous imaging of four neutrophils serine proteases (NSPs) in human blood samples. That study demonstrated for the first time that the NSPs are unevenly distributed within neutrophil granules, potentially indicating their diverse biological functions. Currently this technology is being further expanded for the detection of neutrophil disorders in patients (neutropenia) within a TEAM-NET project from the Foundation for Polish Science.

The application of prof. Drąg's technology has also facilitated the studies on caspases – proteases which orchestrate programmed cell deaths such as apoptosis and recently characterized and heavily investigated pyroptosis. Thanks to apoptosis, damaged and unwanted cells, such as cancer cells, are removed from the organism in an immunologically silent manner. Therefore, dysregulation of this process contributes to the uncontrolled expansion of cancer cells. Over the past few decades, apoptosis has attracted substantial attention from both academia and pharma, as the understanding of this process may lead to new apoptosis-based anticancer

therapies. Recently, prof. Drag with his team developed a series of very selective activity-based probes, which can detect the activity of individual caspases in living cells, providing new mechanistic insight into how caspases are organized within the apoptotic network.

In their research, prof. Drąg's team currently collaborates with over 30 research groups from academia worldwide, as well as with biotech and pharmaceutical companies.

The technology developed in prof. Drąg's laboratory may find, numerous applications in personalized/modern medicine and pharmacology. His group is currently working on the development of new chemical tools for studying medically important proteases, such as the proteases from the Zika, Dengue and SARS viruses, as well as other proteases that are involved in the development of so called lifestyle diseases. In this context HyCoSuL technology holds a great potential to be used as a platform for the generation of new peptides, that can be utilized in a scaffold-based drug discovery.

The future directions of prof. Drąg's research path is to use HyCoSuL for the development of ultraselective chemical probes to be applied in the clinical tests for an early diagnosis of disease and also for the precise detection of proteases-rich disease lesions during surgical interventions, that may help surgeons to improve the surgical procedures.

Dominika Wojtysiak-Łańska
The Foundation for Polish Science
Programme Promotion and External Cooperation Section