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PRESS RELEASE

ORGANIC REACTIONS IN LIVE CELLS

A new fluorogenic click reaction for selective cell-labeling

Prague, January 18, 2017 – Fluorescent probes are an indispensable tool in biological research. They enable the study of biological processes and the specific biomolecules involved in them. Particularly important are probes that become fluorescent only when they react with the biological target of interest. However, the development of such tools is difficult and complex chemical synthesis is often needed for their preparation. Dr. Milan Vrábel and his team from the Institute of Organic Chemistry and Biochemistry in Prague (IOCB Prague) have now developed a novel chemical reaction, which significantly simplifies the whole process. One example of this powerful methodology allows for the imaging the place of action of anti-cancer drugs in live cancer cells almost in real time.

Existing methods for the synthesis of fluorogenic compounds require complex structures, so-called fluorophores, which are often prepared using inefficient, multistep synthetic methods. Milan Vrábel and his group at IOCB Prague have now developed a new fluorogenic click reaction, which enables the selective labeling of cell structures and biologically active substances directly in live cancer cells. In comparison to existing techniques, the new method uses relatively simple starting compounds. In addition, small molecular tuning of the starting compounds results in complete color control of the reaction products in an expedient manner.

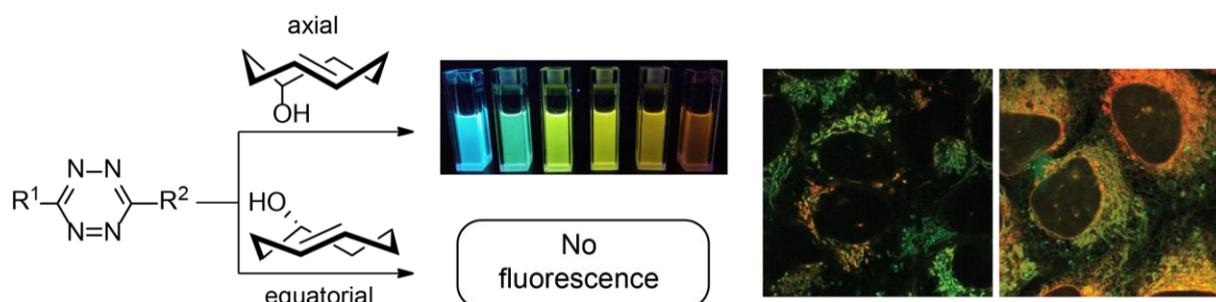


Fig. 1. By using simple starting compounds it is possible to influence the course of the reaction toward the formation of products having different colors.

Another substantial advantage is that the colored products are formed directly upon the reaction of the starting compounds. This leads to a significant reduction in undesired background signals, which is a frequent problem when using classical fluorescent probes.

The power of this methodology is exemplified in the selective labeling of different cellular organelles, such as mitochondria, which play an essential role in many biochemical processes. Another important application of the described chemistry is the visualization of therapeutics at their place of action which can be done nearly at real time due to the fast reaction rate. This could be applied to development of

better-targeted drugs which are active only at the place where they are needed, thus reducing the side effects and enhancing their therapeutic effect.

The scientists from IOCB Prague have published their findings in the prestigious scientific journal *Angewandte Chemie*: Vázquez, A., Dzijak, R., Dračinský, M., Rampmaier, R., Siegl, S. J. and Vrábel, M. Mechanism-Based Fluorogenic trans-Cyclooctene–Tetrazine Cycloaddition. *Angew. Chem. Int. Ed.* **2017**, *56*, 1334–1337. doi:10.1002/anie.201610491

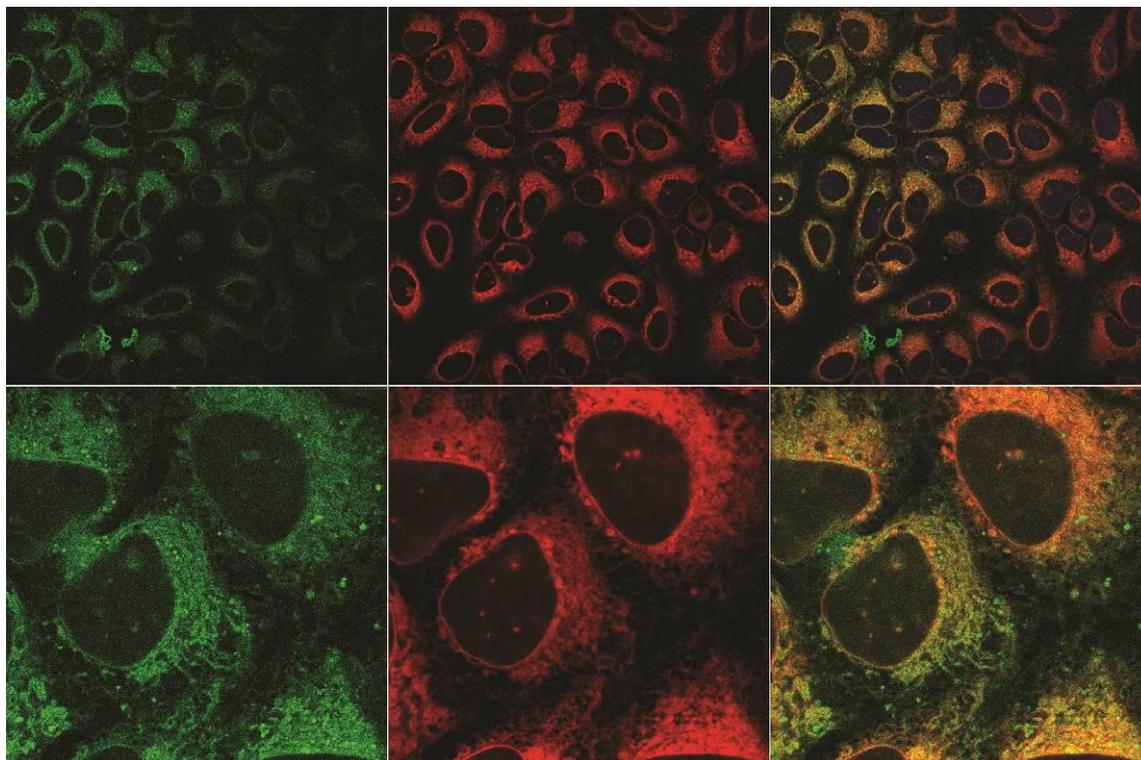


Fig. 2. Our new fluorescent probes allow for the visualization of the place of action of an anti-cancer drugs (such as taxol in microtubules), directly in live cancer cells.

Milan Vrábel, Ph.D. (www.iocb.cz/vrabel) established his group at the IOCB Prague in 2014. In 2016 he received the prestigious 5-year starting grant from the European Research Council (ERC) with a donation of € 1.4 million. His group combines modern synthetic organic chemistry with chemical biology tools and combinatorial library synthesis to create hybrid biological systems with improved features and unique functions. Our main goal is to provide new tools in medicine and to develop small molecule-biomolecule conjugates as next generation therapeutics and bioanalytics.

Institute of Organic Chemistry and Biochemistry of the Czech Academy of Sciences (IOCB Prague) is a leading scientific institution in the Czech Republic, recognized internationally. Its primary mission is basic research in the fields of chemical biology and medicinal chemistry, organic and material oriented chemistry, chemistry of natural compounds, biochemistry and molecular biology, physical chemistry, theoretical chemistry, and analytical chemistry. The Institute's emphasis on interaction between chemistry and other sciences leads frequently to medicinal, pharmaceutical and other applications. An integral part of the mission of the Institute is to transfer the scientific results into assets which help people to live better lives.

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