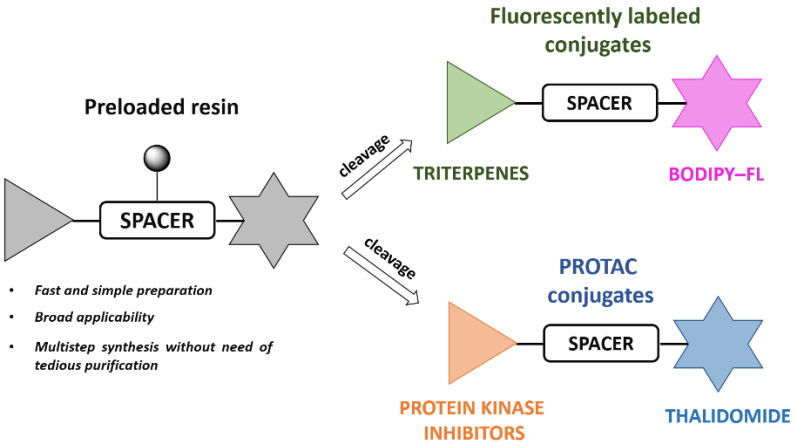
Playing with Properties of Biologically Active Compounds: High-throughput Conjugation of Drug-Like Molecules for Chemical Biology

Soňa Krajčovičová, Miroslav Soural

Department of Organic Chemistry, Faculty of Science, Palacky University, Tr. 17. Listopadu 12, 771 46 Olomouc, Czech Republic

e-mail: sona.krajcovicova@upol.cz

Chemical biology is considered as one of the most progressive interdisciplinary fields in modern science, since it combines the application of chemical and biological techniques to prepare (or structurally modify) small molecules and determines their behavior in various biological systems. However, it is questionable, if synthesis of small, potentially interesting compounds, is the only way how to find suitable biologically useful probes. In this regard, conjugation can significantly improve pharmacological properties of drug-like small molecules to obtain more selective ligands of certain biological targets. As such examples can serve the conjugates of compounds of interests with fluorescent dye (BODIPY-FL® in our case) to visualize molecules in cells using a fluorescent microscopy (applied in the field of cytotoxic terpenes)[1] or heterobifunctional PROTAC (proteolysis targeting chimeras) conjugates with thalidomide moiety, which are able to bind two specific proteins with subsequent targeted degradation (applied in the field of protein kinases inhibitors).[2] We recently developed the high-throughput synthetic approach, which allows fast and simple preparation of desired conjugates without need of tedious purification. Our concept of preloaded resins is broadly applicable not only for abovementioned ligands, but also for different types of compounds possessing suitable functional groups.[3] In this lecture, the synthetic concept utilizing solid-phase synthesis and *in vitro* properties of target conjugates will be reported.



References:

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(3) Soural, M.; Hodon, J.; Dickinson, N. J.; Sidova, V.; Gurska, S.; Dzubak, P.; Hajduch, M.; Sarek, J.; Urban, M. *Bioconjug. Chem.* **2015**, *26*, 2563–2570.