Photopharmacology: Towards Light-Controlled Therapy

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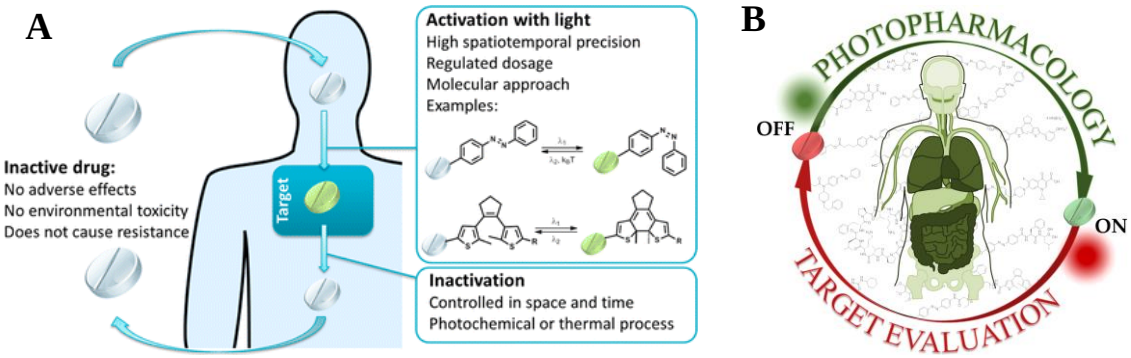
Current pharmacological treatments relay on using bioactive compounds that evoke a response by interacting with molecular targets in the human body. The selectivity of this interaction is crucial and the lack of it leads to the emergence of severe side-effects in the body and toxicity in the environment.

To solve this problem, drugs could be introduced whose activity could be reversibly switched on demand. The aim of this presentation is to describe the recent concept of photopharmacology (Figure A),[1,2] which is currently being developed and applied *i.a.* in our labs[1–5] to precisely control the activity of drugs using light.



The key properties of drugs, such as their distribution and interaction with their molecular targets, are directly influenced by their molecular structure. Photopharmacological agents are designed by the modification of bioactive molecules with molecular photoswitches, i.e. moieties that change their structure upon irradiation with light. These changes are directly translated to the differences in drug activity.

The presentation will describe: 1) chemotherapeutic inhibitors of histone deacetylases, which show up to 40x increase in potency upon light irradiation;[3] 2) quinolone-based antibiotics that can be activated with light, designed to avoid the emergence of antibiotic resistance in the environment[4] and 3) light-regulated bacterial quorum sensing inhibitors used for photocontrol of gene expression.[5]

The aspects of molecular design,[1-5] synthesis,[6] optimization, photochemical characterization[7] and biological activity will be discussed. An outlook on the prospects of bringing photopharmacology to clinical application, including the milestones and future landmarks, will be presented, together with the evaluation of organs in human body with regards to the feasibility of light-based therapy.[2]

[1] *J. Am. Chem. Soc.* **2014**, *136*, 2178–91.
[2] *Angew. Chem. Int. Ed. Engl.* **2016**, *55*, 10978-99.
[3] *Chem. Eur. J.* **2015**, *21*, 16517–24.
[4] *Nature Chem.* **2013**, *5*, 924–8.
[5] *Chem. Sci.* **2015**, *6*, 3593–3598.
[6] *Angew. Chem. Int. Ed.* **2016**, *ASAP*.
[7] *Nature Communications* **2016**, *7*, 12054.