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Photopharmacology: Where light and molecules meet crystallography

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Azobenzene photoisomerization can be chemically implemented in protein ligands to actuate on biological receptors and to manipulate their activity with light. Azobenzene small molecule photoswitches can be designed and synthesized to serve for real-time regulation of receptors with high spatiotemporal accuracy using specific illumination patterns. The basis for this is a different interaction mode of the ligand isomers with the biological receptor. Therefore, light can be used for a precise control of physiology, on/off drug activation and targeting localized organs in free behaving animals. Strikingly, the photomolecular isomerization can also be employed in structural studies. Photoswitchable ligands co-crystallized with biomolecules can be used for triggering molecular actions in the crystal upon illumination. The bound ligand can be very fast photoisomerized, sharply generating a new state, which induces a receptor rearrangement that can be experimentally measured. This light switch in the crystallized receptor, which is reminiscent of some photon activated endogenous receptor systems, opens unprecedented possibilities to measure structural changes at atomic resolution and at very short-time scale. This approach will involve cooperative work of chemists, biologists, physicists and engineers, and may open a new perspective in dynamic studies of biological processes that can change our understanding of life and applied to invent radically new therapeutic approaches.

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