Photoswitchable ligands as tools for dynamic modulation of histamine receptors

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Histamine receptors are widely distributed throughout the body and respond (in a paracrine/autocrine manner) to local increases in histamine. Hence, it would be therapeutically advantageous to only locally influence histamine receptors rather than systemic targeting of the receptor to avoid unwanted side effects. Temporal and spatial control of drug effects can be induced utilizing photoswitchable ligands. Photoswitchable ligands can reversibly photo-isomerize from the *trans* to the *cis* isomer upon illumination with specific wavelengths. The resulting conformational change in the ligand may result in distinct changes in binding affinity and/or intrinsic activity of the isomer for the receptor. To this aid, we have developed and characterized a toolbox of photoswitchable ligands for the different histamine receptor subtypes that enables dynamic optical control of their activity with high temporal resolution. Moreover, the option to locally modulate the receptor activity with light opens opportunities to investigate the local role of histamine receptor signaling *in vivo*.