CONTROLLING THE CIRCADIAN CLOCK WITH HIGH TEMPORAL RESOLUTION THROUGH PHOTODOSIMETRY

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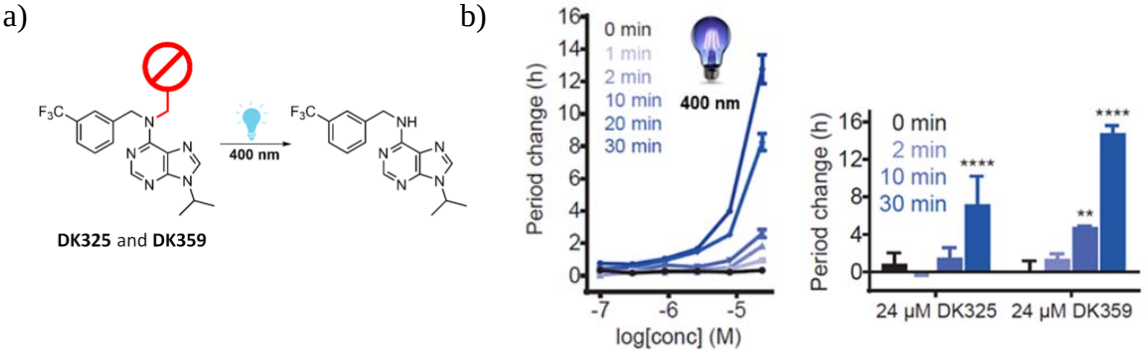
Inspired by the crucial role of circadian clock disruption in disease development,[1] during the last decade chemical biology studied how to adjust cellular clocks using small molecule modifiers.[2] Unfortunately, these modifiers are still facing a big drawback when *in vivo* application is needed: due to the similarity in cellular regulation of clocks, besides curing the disrupted biological rhythm they would affect all the others, healthy rhythms in other cells. To overcome this problem, a potential strategy would be photocaging - based on the regulation of a compound`s bioactivity with light, which can be delivered precisely in space and time.[3]

Here, we show for the first time the possibility to control the circadian rhythm with high temporal resolution. Lengthening of the circadian period was achieved in mammalian cells, tissue, and zebrafish just by choosing an interval of visible light irradiation (400 nm) in order to release longdaysin – a known CKI inhibitor and compound that exhibits a drastic effect on the circadian period.[4]



Scheme 1. a) Photo-deprotection of the protected longdaysin; b) correlation diagram of period lengthening, concentration, and light exposure time in cells and tissue explant.

[1] Science, 2005, 308, 1043; Nature, 2010, 466, 627; Proc. Natl. Acad. Sci., 2006, 103, 9327

[2] Science, 2012, 337, 6098; Angew. Chem. Int. Ed., 2015, 54, 7193

[3] Chem. Rev. 2013, 113, 119; Chem. Soc. Rev., 2015, 44, 3358

[4] PLoS Biology, 2010, 8, e1000559