

Light-activated drugs provide localized medicine without side effects

September 9 2021



Team led by Professor Francisco Ciruela. Credit: UB-IDIBELL-UBNeuro

Photopharmacology is an emerging area of science based on the development of photosensitive drugs, that is, drugs that activate with light. A team from IDIBELL and the University of Barcelona has

worked on two treatments based on this innovative technology: a morphine derivative that does not create addiction and a new treatment against psoriasis. The same group has used this technology to determine the role of adenosine in pain transmission.

This innovative technology combines drugs with molecules that work as switches, and with the action of light, modify its structure, and therefore its biological activity, with light. This modulation allows the activation of the drugs in the desired place, time and intensity, focusing on its action and avoiding side effects in other tissues, where these do not act.

The Research Group on Neuropharmacology and Pain of the Bellvitge Institute for Biomedical Research (IDIBELL), the Faculty of Medicine and Health Sciences and the Institute of Neurosciences (UBNeuro) of the UB, led by Professor Francisco Ciruela, has presented a photo-activable morphine derivative and a photopharmaceutical drug to treat psoriasis and a photocommutable derivative from adenosine that allows researchers to study pain transmission.

Non-addictive morphine

At the moment, morphine and other derivatives of opiates are the most widely used treatments to alleviate pain. Although these drugs are very effective, many present severe side effects such as addiction and dependence. Moreover, patients can develop tolerance to the [analgesic effects](#), which makes them increase the dose. In the United States, it is estimated that more than 70,000 people die from an overdose of opiates. 30% of the patients who are prescribed with these drugs do not take them following the right instructions, and this results in 10% of the patients ending up with a dependency on this drug.

The team led by Francisco Ciruela, in collaboration with Amadeu Llebaria (IQAC-CSIC, Barcelona), has designed, synthesized and

characterized a photosensitive morphine derivative that can be activated through light with high precision. This morphine has proved to have an analgesic effect on mice. In addition, the remote and local activation of this compound showed to prevent the tolerance to the analgesic effect and appearance of the drug-dependency. The study has been published in the *British Journal of Pharmacology*.

"Pharmacology enabled us to create an opiate-based therapeutic approach with an optimal risk-benefit ratio," says Ciruela. "This photosensitive morphine has proved an analgesic efficiency which is as effective as the original one, but avoiding addiction, tolerance and general side effects which are usually caused by opiate derivatives," adds the expert.

A solution for psoriasis

In the journal *Pharmacological Research*, researchers have presented a solution for psoriasis based on photopharmacology. In this case, they designed, in collaboration with Professor Kenneth Jacobson (NIDDK, NIH, Bethesda, U.S.), a light-activated molecule that binds the adenosine A3 receptor, inducing a powerful anti-inflammatory effect.

Psoriasis is a chronic skin disease which affects 2% of the population and is expressed mainly through cutaneous symptoms such as dryness, itchiness, scaly skin, spots and abnormal plaques, caused by an overgrowth of the keratinocyte skin cells and an aberrant immune response. The available treatments are mainly focused on the alleviation of symptoms, not the cause of the disease, and severe cases undergo modulating treatments of the immune system that have severe side effects due to the generalized immunosuppression.

"The photodrug we present is capable of preventing psoriasis symptoms in mice. In addition, its local photoactivation in the affected skin

prevents the appearance of [side effects](#) derived from the anti-inflammatory systemic potential of the [drug](#)," notes Marc López-Cano, researcher at the UB and IDIBELL, and first author of both articles.

A tool to study pain transmission

The researchers have developed a photocommutable derivative of adenosine, in collaboration with Professor Dirk Trauner, from the University of New York (U.S.), which enabled them to map the contribution of the several adenosine receptors in pain transmission.

Adenosine is a neuromodulator of the cells in the nervous system. It can act as an endogenous analgesic, but the adenosine receptors that cause this effect are still unknown. Now, and thanks to this photopharmacological tool, researchers have determined the [adenosine](#) receptors that cause the analgesic effect, both at a peripheral and a central level. This information will be useful for designing and synthesizing selective adenosynergic drugs to manage the peripheral and central pain. Results have been recently published in the journal *Bioconjugate Chemistry*.

More information: Marc López-Cano et al, Remote local photoactivation of morphine produces analgesia without opioid-related adverse effects, *British Journal of Pharmacology* (2021). [DOI: 10.1111/bph.15645](#)

Marc López-Cano et al, Optical control of adenosine A3 receptor function in psoriasis, *Pharmacological Research* (2021). [DOI: 10.1016/j.phrs.2021.105731](#)

Katharina Hüll et al, Optical Control of Adenosine-Mediated Pain Modulation, *Bioconjugate Chemistry* (2021). [DOI: 10.1021/acs.bioconjchem.1c00387](#)

Provided by University of Barcelona

Citation: Light-activated drugs provide localized medicine without side effects (2021, September 9) retrieved 26 April 2024 from

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