Esteve, UB and IDIBELL develop a new technology for screening drugs with potential analgesic

Predicts the analgesic activity of the molecules before being tested in animal models and thus save time and money in the search for new drugs

Researchers of the Neuropharmacology and Pain research group of the Bellvitge Biomedical Research Institute (IDIBELL), the University of Barcelona and Esteve have developed a new technology that allows to find out which the analgesic drugs are before being tested in animal models. This also allows a significant savings of time and money in the search for new medicines really effective in the treatment of pain.

Traditionally, in the development of new analgesic drugs the effectiveness of these molecules has been demonstrated using animal models of pain, a heavy, expensive and sometimes little illuminating from the pharmacological point of view process. For this reason, in recent years the development of new methodologies is a challenge. "We are talking about thousands of drugs. That's why, before testing in preclinical models of pain, ie , in animal models, it would be good to do a screening of the activity of these molecules to separate those who have a greater antinociceptive potential," explained Dr. Ciruela from the Neuropharmacology and Painresearch group at IDIBELL and professor at the University of Barcelona (UB).

The study led by Dr. Ciruela describes a new technology that allows to determine the analgesic activity of these drugs before being tested in animal models. " We have developed a biosensor based on echoes Fluorescence Resonance Energy Transfer (FRET) that allows users to catalog in a simple system (cells in culture) ligands in Sigma -1 receptor agonists and antagonists " says the researcher.

Thus, the experiments performed by ESTEVE and Dr. Cireula (IDIBELL-UB) with known drugs have established a direct correlation between the biosensor FRET signal in response to these drugs and the analgesic efficacy of the same in an animal model of pain. According to the results, while -1 Sigma receptor activator, ie, agonists, the FRET biosensor signal decreases and exhibit low analgesic efficacy, antagonists or blockers of the receptor, increases the FRET signal and have a high analgesic efficacy in animal models of pain.

"With such a defined pattern" explains Dr. Cireula "we can test a new molecule and make a prediction of its analgesic behavior. Thus, if you the FRET biosensor is low, ie, if it behaves as an agonist,it will be expected not to have analgesic effects in the animal model of pain, but if you increase the FRET -acting antagonist- will potentially a maximum analgesic effects and therefore be a good candidate to be tested in vivo . "

This new technology has been patented , as explained by the researcher, and although it is too early to take full advantage because "we are currently doing FRET measurements with drugs one by one" , is soon expected to be applied extensively to the development of analgesic antagonists Sigma-1 receptor. So , right now the system is expected to robotize it , with the aim of developing a tool that would be technically known as high- throughput screening, ie, a method for testing many drugs quickly and efficiently.

Analgesia, an area with many medical needs

The pharmacology of pain there are two main groups of drugs: nonsteroidal antiinflammatory drugs (NSAIDs) and opioids . Each has different mechanisms of action with an analgesic ceiling and unequal side effects. While NSAIDs (eg ibuprofen) have a low to moderate analgesic potency and moderate side effects , opioids (eg morphine) are very potent analgesics and their use may result in the occurrence of serious adverse effects. Therefore, there is an important gap analgesic, not only as to present a risk-benefit profile favorable for the treatment of moderate -high pain but also in the approach to pain , which often reference drugs are not effective (eg neuropathic pain).

Esteve focuses part of its R & D in search of active molecules for the treatment of neuropathic pain and pain in patients treated with opioids in order to achieve good efficacy and better tolerance and a decrease in the frequency and severity of adverse effects associated with this class of drugs . Thus , blocking the Sigma -1 receptor with specific antagonists is proposed as a new mechanism of action for the treatment of pain in an area that just presents a significant need for new therapies. Thus , in addition to a selective antagonist of Sigma -1, E -52862 receptor, which is currently undergoing clinical trials , Esteve has a library of molecules with potential activity on this receptor.

Referència de l'article

Gómez-Soler,M., **Fernández-Dueñas**, V., **Portillo-Salido** E., **Pérez**, P., **Zamanillo**, D., **Vela**, J.M., **Burgueño** J. and **Ciruela** F. **Predicting the Antinociceptive Efficacy of σ1 Receptor Ligands by a Novel Receptor Fluorescence Resonance Energy Transfer (FRET) Based Biosensor**. ***J. Med. Chem.***, 2014, ***57*** (1), pp 238–242