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Press release

## **Antipain, antidepressant – an “all-in-one” molecule**

**Institut Pasteur scientists associated with the CNRS and a team from the ETAP-Applied Ethology neuropsychopharmacology research center based in Vandoeuvre-lès-Nancy have reported the analgesic and antidepressant effects of Opiorphin, a hormone messenger naturally secreted in humans that was discovered at the Institut Pasteur in 2006. The molecule has proved to be as potent as morphine in experimental (animal) models, with considerably milder side effects. It is also as effective as imipramine, an antidepressant available on the market, but does not elicit imipramine’s major side effects. Given that pain and depression are often linked, scientists hope to be able to develop a single drug candidat based on this molecule that could treat both disorders.**

Opiorphin is the name that Catherine Rougeot and her team from the Structural and Cellular Biochemistry Unit (Institut Pasteur/CNRS) gave to the molecule with remarkable properties.. In two articles published in the *Journal of Physiology and Pharmacology* in June and August 2010 respectively, the scientists present the results of their research on the characterization of the molecule’s painkilling and antidepressant potencies.

In cooperation with the ETAP team from the Nancy-Brabois Technopole, the Institut Pasteur scientists demonstrated *in vivo* that, for the same doses, Opiorphin produces a comparable analgesic potency as morphine, in both thermal and mechanical acute pain and in chemical-induced tonic pain. The side effects are considerably milder than those of morphine: Opiorphin does not induce tolerance (doses do not have to be increased to obtain the same antinociceptive) or does not cause constipation, and it has a much lower potential of addiction (the potential emergence of psychological dependence).

The antidepressant properties of Opiorphin are also particularly potent – in animal models, the molecule at the same anti-pain titration is as effective as imipramine, a potent compound used clinically. It does not induce side effects, such as sedation or hyperactivity and does not affect learning acquisition and memorization, as some anti-depressant drugs are criticized for doing.

Pain and depression are often linked: depressive disorders frequently amplify pain sensitivity, and *vice versa* – chronic pain is often associated with depressive disorders. A drug candidat based on Opiorphin, effective at the same doses against both pain and depression, would be beneficial as it could treat simultaneously both disorders. In their efforts to develop a therapeutic application, scientists are currently investigating on the chemical optimization of synthetic Opiorphin derivatives, in order to improve its stability and thus to increase its bioavailability and duration of action. Only once these essential steps have been completed it will be possible to

plan the first clinical trials, so that the therapeutic potential of Opiorphin or its synthetic derivative can be properly assessed.

### **A short history of Opiorphin**

It all began in 1988. A team of scientists led by François Rougeon at the Institut Pasteur had just identified a gene potentially coding for a new hormone precursor. Adopting an original post-genomic pharmaco-chemical approach, based on the product of this gene, Catherine Rougeot identified a new hormone messenger in rats called Sialorphin. The molecule then demonstrated its potent analgesic effect – *in vivo*, it was as effective as morphine. Sialorphin acts by blocking the action of enzymes responsible for inactivating enkephalins, highly potent endogenous antipain molecules. The researchers continued their work by seeking the functional analog of Sialorphin in humans. In 2006, they identified Opiorphin. The results of the functional tests led the scientists to confirm Opiorphin's role in activating endogenous enkephalin-dependent signaling pathways, and demonstrate its exciting painkilling and antidepressant properties.

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### **Source**

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**Human Opiorphin is a naturally occurring antidepressant acting selectively on enkephalin-dependent delta-opioid pathways, *Journal of Physiology and Pharmacology*, 2010, 61(3): 355-362.**

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**Systemically active human Opiorphin is a potent yet non-addictive analgesic without drug tolerance effects, *Journal of Physiology and Pharmacology*, 2010, 61(4): 483-490.**

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