



SELECTED OPPORTUNITIES IN GERONTOLOGY

METHODS AND PHARMACEUTICAL COMPOSITIONS FOR THE
TREATMENT OF POST-OPERATIVE COGNITIVE DYSFUNCTION
(BIO 15529)

Product factsheet

Preclinical

▶ **Target:**

- ◆ Apelin receptor (APJ)

▶ **Product:**

- ◆ APJ receptor agonist

▶ **Application:**

- ◆ Post-operative cognitive dysfunction

▶ **Technology:**

- ◆ Peptides, apelinomimet, small molecules, antibodies, aptamers...

▶ **Rational / POC:**

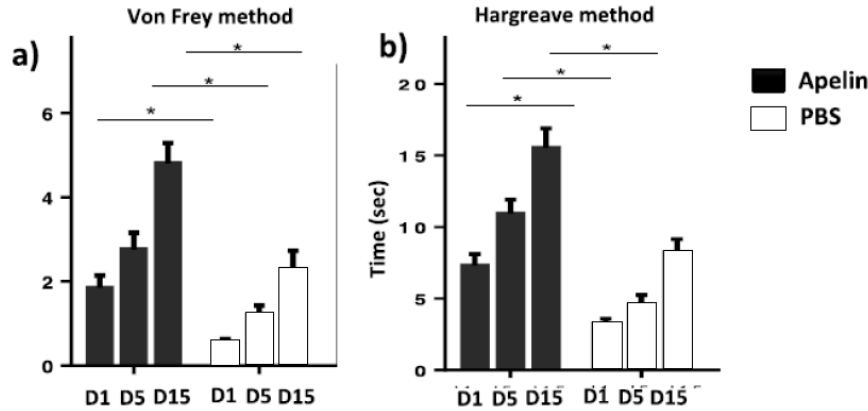
- ◆ Apeline reduces pain, inflammation and postoperative cognitive impairment in a mouse model of closed tibial fracture
- ◆ Apelin is still protective in the same model with old mice
- ◆ Plasma apeline concentration is reduced in patients at D+1 after a programmed hip replacement surgery and a normalization is observed after 6 days

▶ **Patent and publication:**

- ◆ Patent PCT/EP2017/053308: METHODS AND PHARMACEUTICAL COMPOSITIONS FOR THE TREATMENT OF POST-OPERATIVE COGNITIVE DYSFUNCTION

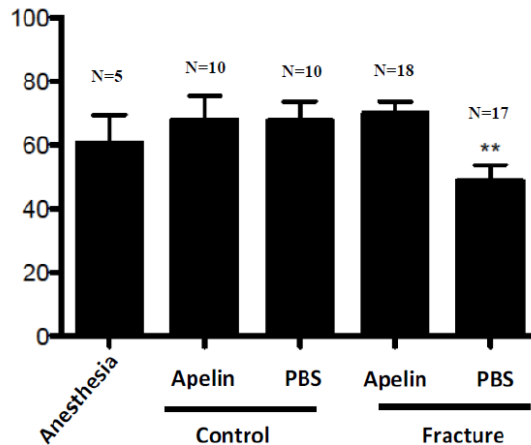
Proof of concept

► Pain is reduced by apelin treatment



Pain and nociception measured by Von Frey or Hargreave's techniques are significantly decreased by apelin treatment as respectively shown in Figures a and b.

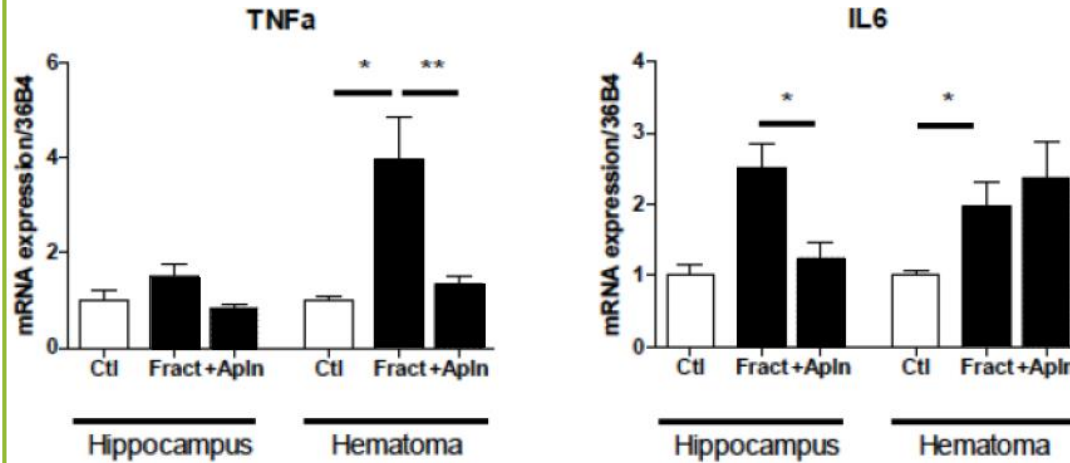
► Daily treatment with apelin increases the freezing carried out in mice



Postoperative, the operated mice developed cognitive impairment. Third days post-surgery, the operated animals showed freezing rate statistically lower than those of non-operated animals. The operated mice that received a daily injection of apelin had a freezing rate increased compared to mice receiving operated saline injections. The non-operated mice treated by apelin did not display change in their rate of freezing.

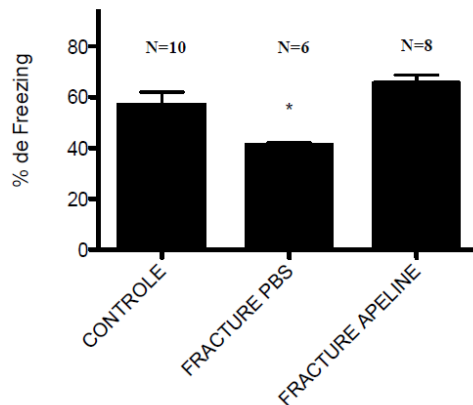
Proof of concept

► Inflammatory status



Apelin treatment decreased hematoma TNFα mRNA and hippocampus IL-6 mRNA expression in fractured mice.

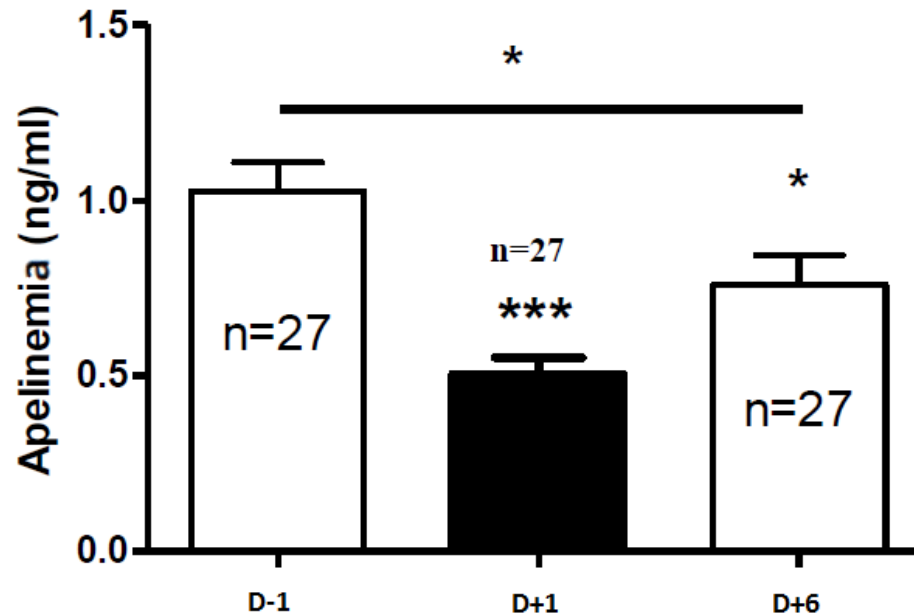
► Apelin increases the freezing carried out in aged mice



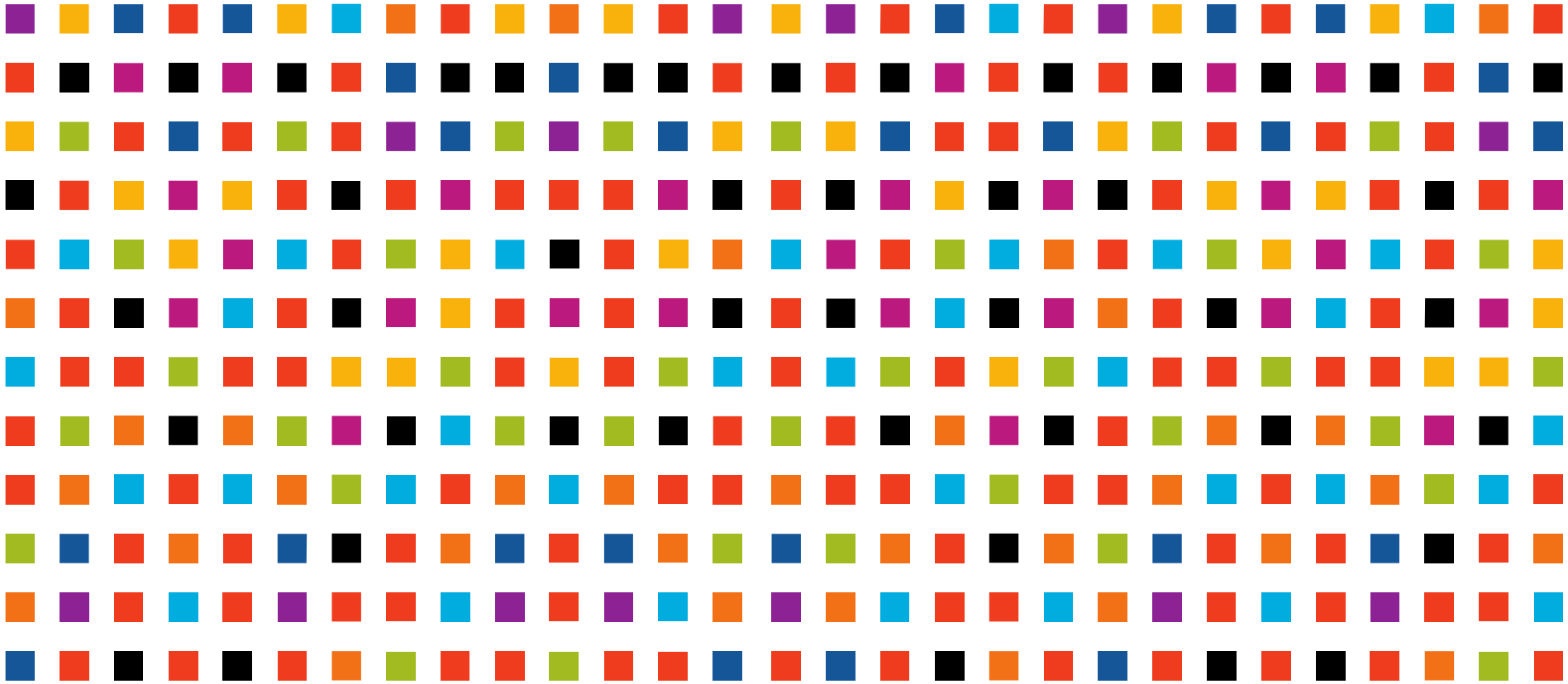
*Percentage of freezing in aged mice. Twenty month old male C57Bl6/j mice were fractured with (fracture apelin) or without (fracture PBS) an i.p treatment of apelin (0.5nmol/kg) before and during 3 days after the fracture. After 3 days, animal hippocampal memory was tested by fear conditioning test. N=6 to 10, * p<0.05 compared to control.*

Proof of concept

► Plasma apelin variation in response to surgery in human



Plasma apelin variation before and after a programmed hip replacement surgery. Blood was collected in patients 24 h before the surgery (D-1) or 24h or 6 days later (D+1 and D+6). Plasma apelin was measured by a commercial ELISA test. In this study, patient are 60 years old and over.



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