

Inleptin Therapeutics

developed by faculty from
The George Washington University and Johns Hopkins University

Technology Summary

- ▶ Opioid overdose kills 130 people in the United States every day (<https://wonder.cdc.gov>)
- ▶ Opioid deaths are mainly caused by opioid induced respiratory depression (OIRD)
 - ▶ Obesity and comorbid risk factors (sleep disordered breathing) increase risk of OIRD
 - ▶ The opioid antidote, naloxone, can treat OIRD, but reverses analgesia and induces opioid withdrawal
- ▶ Our Solution: Intranasal Leptin
 - ▶ Natural Adipose tissue produced hormone
 - ▶ Regulates energy homeostasis / metabolism
 - ▶ Receptors in respiratory center of the brain
 - ▶ Intranasal (IN) route used to deliver to the brain
 - ▶ Brain delivery reverses sleep disordered breathing
 - ▶ IN leptin treatment after opioid dosing can prevent OIRD and reduce mortality

Challenges with current therapies

- ▶ Naloxone is the only drug available:
 - ▶ Downside 1: Reverses analgesia
 - ▶ Downside 2: Induces opioid withdrawal
- ▶ Patients need a preventive treatment for sleep-related OIRD that does not have these problems

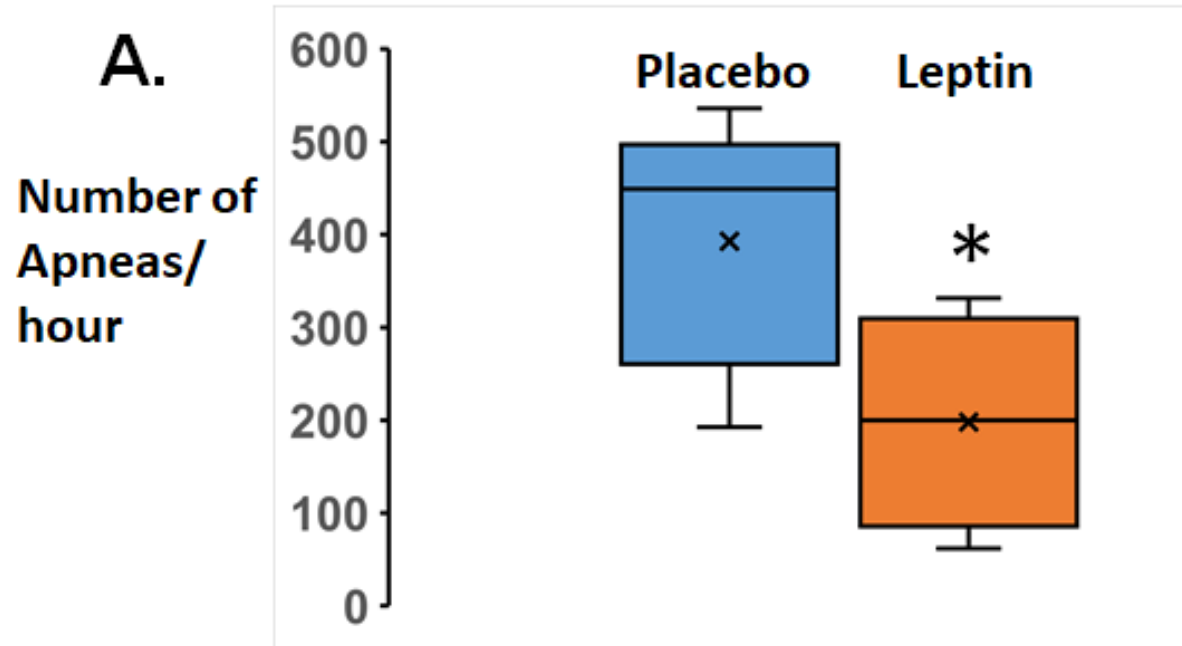


Intranasal Leptin Treatment

- ▶ IN Leptin prevents OIRD (in mouse studies)
- ✓ Ease of administration
- ✓ Safer use of high-dose opioids in obese opioid tolerant patients
- ✓ No interference with analgesic properties
- ✓ No withdrawal symptoms

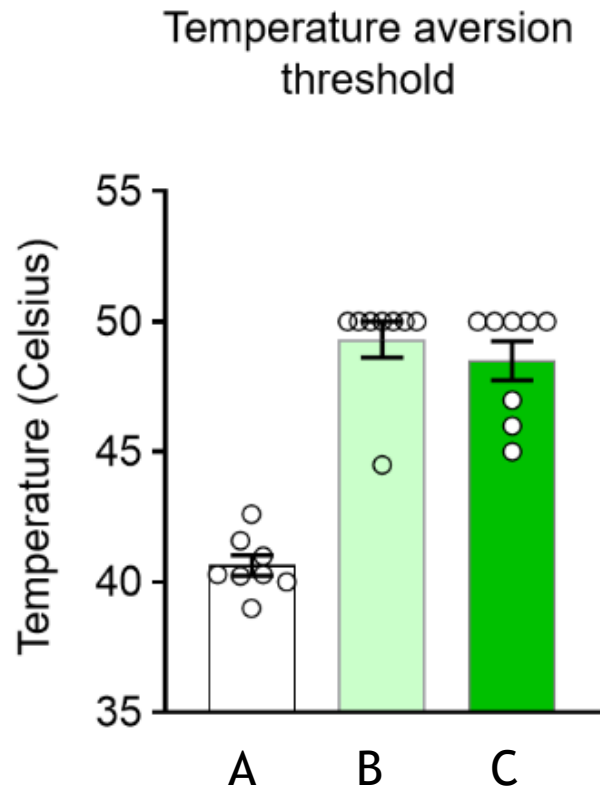


IN Leptin reduced # of apneas per hour in obese mice



The effect of chronic IN leptin on the number of apneas per hour (A) in morphine-tolerant diet-induced obese (DIO) male mice. Mean (x) and median (the line) are shown inside the boxes outlining the 1st and the 3rd quartile and the whiskers showing the highest and the lowest values. *, $p < 0.05$.

Leptin did not reduce analgesia from morphine in obese mice



A = Control
B = morphine and vehicle
C = morphine and leptin

Thermal place preference protocol on diet induce obese mice. Two plates change their temperature, and mouse position is tracked over time. Animal exposed up to 4 times to a temperature rise to noxious heat. Aversion temperature where animal escapes the plate is recorded.

How big is the market?

- ▶ Nearly 70,000 Americans died of an opioid overdose in 2020, a major increase from 50,504 deaths the year before (<https://www.cdc.gov/nchs>)
- ▶ Patients with one or more OIRD events had a longer length of stay (6.4 vs. 5 days) and had 17% higher hospital costs than those who did not have an episode (<https://doi.org/10.1186/s12871-021-01307-8>)
- ▶ Bottom up market estimate
 - ▶ US adults = 260 million
 - ▶ Hospitalizations per year = about 10% of population
 - ▶ Obese = 40% of population
 - ▶ Chronic opioid users = 2%
 - ▶ Average hospital stay = 5 days
 - ▶ Assume 1 dose per day of IN Leptin
 - ▶ Price per dose = \$2,000 (comparable to injected Leptin Myalept (\$5,788 for 11mg))

**Potential Market
\$2 billion**

Competition

- ▶ **Naloxone infusion:** the only treatment currently available to reverse OIRD
- ▶ Generic naloxone can cost between \$20 and \$40 per dose, while Narcan® can cost around \$130 to \$140 for a kit that includes two doses
- ▶ Naloxone market size stood at \$320 Million in 2021
- ▶ **Non-opioid medications for chronic pain:** ibuprofen (Motrin), acetaminophen (Tylenol), aspirin (Bayer), and steroids. (Likely inadequate for hospital procedures)

The Team



- ▶ **David Mendelowitz, Ph.D.**
- ▶ Interim Chair, Department of Pharmacology and Physiology
- ▶ Professor, Pharmacology and Physiology
- ▶ Research Interest: autonomic and respiratory control of brainstem cardiovascular function



- ▶ **Vsevolod Y. Polotsky, MD, PhD**
- ▶ Professor, Johns Hopkins University School of Medicine
- ▶ Research Interest: Obstructive sleep apnea, Hypoxia, Metabolic Syndrome



- ▶ **Carla Freire, Ph.D.**
- ▶ Postdoctoral Research Fellow
- ▶ Department of Pulmonary, JHU
- ▶ Research Interest: Critical Care and Sleep Medicine

The ASK

- ▶ What we are looking for:
 - ▶ Experienced entrepreneur to found a company
- ▶ How far from evaluation of the technology in patients?
 - ▶ Mouse studies are published and in submission
 - ▶ Leptin is already FDA approved for injection. Intranasal will require additional studies.

Closing

- ▶ Intranasal leptin did not interfere with analgesic properties of morphine and no withdrawal symptoms were observed
- ▶ Intranasal leptin as a powerful respiratory stimulant and novel treatment for OIRD
- ▶ Intranasal leptin therapy is safe (in mice) and easy to administer
- ▶ Joint George Washington University and Johns Hopkins University IP: WO2021101814A1 - Intranasal leptin prevents opioid-induced respiratory depression in obesity