Investigating the anti-addiction properties of MP1104, a novel dual kappa & delta opioid receptor agonist

Diana Atigari
Drug Addiction - a BIG problem!

- Major socioeconomic issue
- No FDA approved treatments for psychostimulant drug abuse
- Prescription opioid abuse is a growing problem
The Reward pathway

1. Ventral tegmental area
2. Nucleus Accumbens
3. Prefrontal cortex
Co-localisation of Kappa Opioid and dopamine neurons
Kappa opioid receptors agonists

- Reduce the rewarding effects of drugs of abuse by decreasing dopamine levels in the reward circuitry

- Side effects like aversion, dysphoria, depression limit their clinical development
MP1104 - Is a potent activator of both Kappa & Delta opioid receptors

Hypothesise that mixed kappa agonists, with delta activity may have reduced side effects than pure kappa agonists

Aims:
- To investigate the analgesic effects of MP1104
- To investigate the therapeutic potential of MP1104 in rats trained to self-administer cocaine
MP1104 – Anti-pain effects

- MP1104 at 0.3 and 0.6 mg/kg dose showed longer duration of action.
- MP1104 showed to be more potent than Morphine.
**MP1104** - Activates both Kappa & Delta opioid receptors

**Anti-addiction effects:**
In mice MP1104 blocked cocaine and alcohol Conditioned place preference

**Reduced side effects:**
- No aversion
- No seizures
Evaluate the **Anti-Addiction** effects of **MP1104** in rats using the **Drug self-administration model** – a gold standard preclinical model to measure drug use.
MP1104 at 0.3 & 1 mg/kg attenuates drug-seeking behaviour in rats
Cocaine dose-response self-administration curve

At 0.3 & 0.6 mg/kg MP1104 significantly shifts the cocaine dose-response self-administration curve downwards.
Conclusion

- MP1104 has shown to have anti-cocaine effects by attenuating the effects of cocaine.
- MP1104 has potent analgesic effects with longer action
  - >15 fold more potent than morphine
  - Longer duration of action than morphine
- Potential to be developed as a non-addictive pain medication.
Acknowledgements

Dr Bronwyn Kivell,
Senior Lecturer
Victoria University of Wellington,
New Zealand

Dr Susruta Majumdar
Assistant Attending Chemist
The Gavril Pastemak Lab
Memorial Sloan-Kettering Cancer Center,
New York, USA

Dr Anne Macaskill
School of Psychology,
Victoria University of Wellington

Amy Ewald
David Young
Kelly Paton
Stephen Mathew

All of KK 601 lab