

**Project title:** Mechanistic insights into the role of an orphan receptor, GPR139 and kratom-derived alkaloid (mitragynine) in modulating the anti-addictive effect

## **1. Brief Background of Research Project**

The current opioid epidemic is one of the most severe public health crises globally. Kratom has received attention as an alternative to traditional medicines and replacement therapy for opiate dependence. However, the therapeutic potential of kratom remains to be validated because of its addictive property. GPR139, an orphan G-protein coupled receptor, has recently been shown to interact with the mu opioid receptor (MOR) in the anti-reward centre, habenula and acts as a brake to oppose the effects of opioid drugs. This project aims to test the hypothesis that blocking GPR139 would limit the adverse effects of kratom alkaloid (mitragynine).

This project would help to elucidate a novel mechanism underlying the addictive effect of kratom via GPR139 pathway in the habenula. Further, this would open up the opportunity to use kratom as a safe and effective therapy for opioid abuse.

## **2. Project Description**

GPR139, a poorly understood G-protein coupled receptor, has recently been shown to interact with the MOR and acts as a brake to oppose the effects of opioid drugs. In this proposed study, we hypothesize

- Kratom alkaloid (mitragynine) binds to the MOR in the presence of GPR139
- Blocking GPR139 would limit adverse effects of mitragynine
- Blocking GPR139 would enhance MOR-mediated inhibition of neuronal firing in the anti-reward centre, habenula.

## **3. Objectives**

- i. To examine the binding property of mitragynine to the MOR-GPR139 complex.
- ii. To examine anti-rewarding and anti-withdrawal effects of co-administration of mitragynine and GPR139 antagonist.
- iii. To examine the effect of co-administration of mitragynine and GPR139 antagonist on neural activity in habenula neurons.

## **4. Supervisor / Supervision team**

- i. Dr Satoshi Ogawa  
<https://www.monash.edu.my/jcsmhs/staff/academic/satoshi-ogawa>

- ii. A/Prof Sivakumar A/L Thuraijasingam  
<https://www.monash.edu.my/jcsmhs/staff/academic/sivakumar-thuraijasingam>
- iii. Prof Ishwar Parhar  
<https://www.monash.edu.my/jcsmhs/staff/academic/ishwar-parhar>
- iv. A/Prof Zurina Binti Hassan (USM)

## **5. Eligibility**

*Candidates must meet the minimum admission requirements (academic and English language proficiency) for the research degree. Candidates interested in applying for scholarship must meet the minimum eligibility for scholarship application which is equivalent to a high distinction average (H1/H1E or 1st Class Honours as per Faculty's and Monash's assessment at admission) from a recognized university. Applications for scholarship will go through a rigorous Campus ranking exercise of academic achievement, research publications, and research experience or research-related awards.*

## **6. Required Skills**

- i. Basic biological lab skills (basic cell culture and/or molecular biology experience would be advantageous)
- ii. Standard PC skills (experience in Python would be advantageous)
- iii. Life science background (neuroscience background would be beneficial)