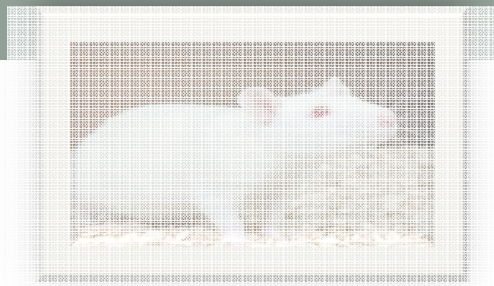
THE EXPRESSION LEVEL OF GLUT-1 RECEPTOR IN THE BRAIN OF NICOTINE - DEPENDENT RAT

Dr. Anggraini Barlian (SITH)

Dr. Kusnandar Anggadiredja (SF)

A. INTRODUCTION



- Nicotine is an addictive substance with devastating effect on health. Smoking habit can lead to nicotine addiction.

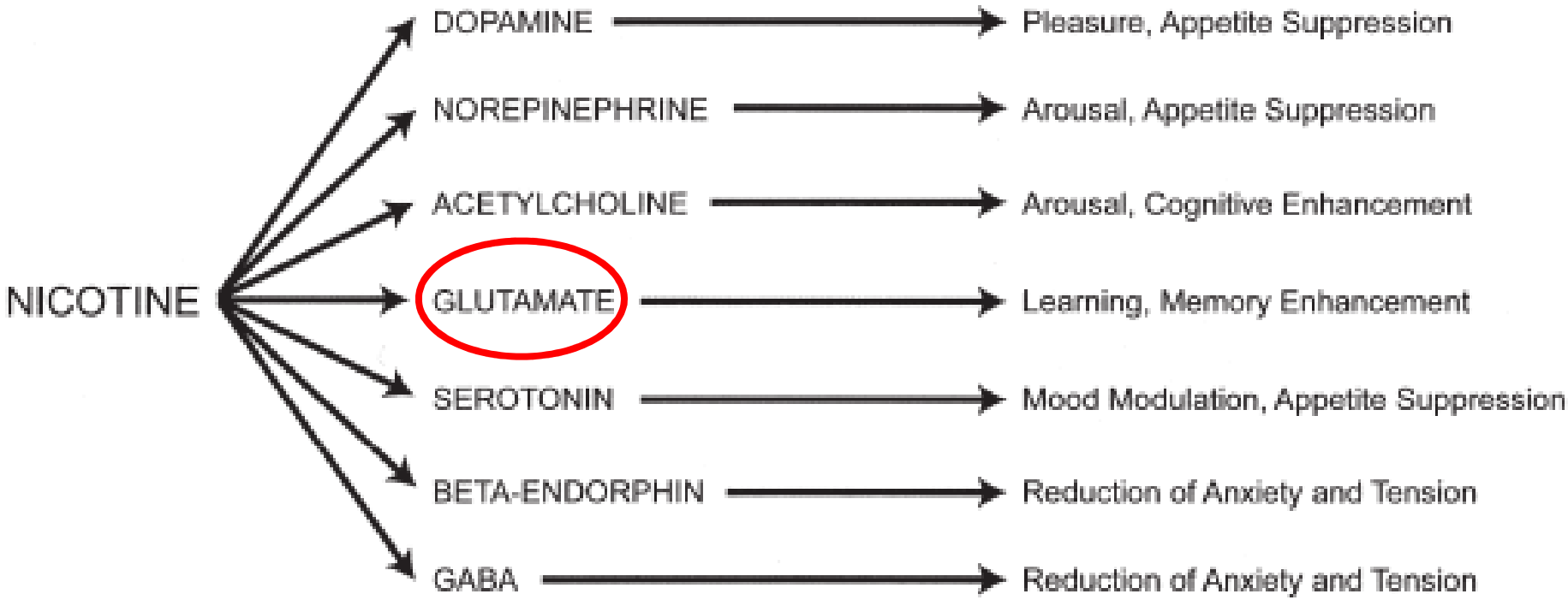
- High risk diseases :
  - Respiration, Cardiovascular, Cancer → ACTIVE/ PASSIVE smokers

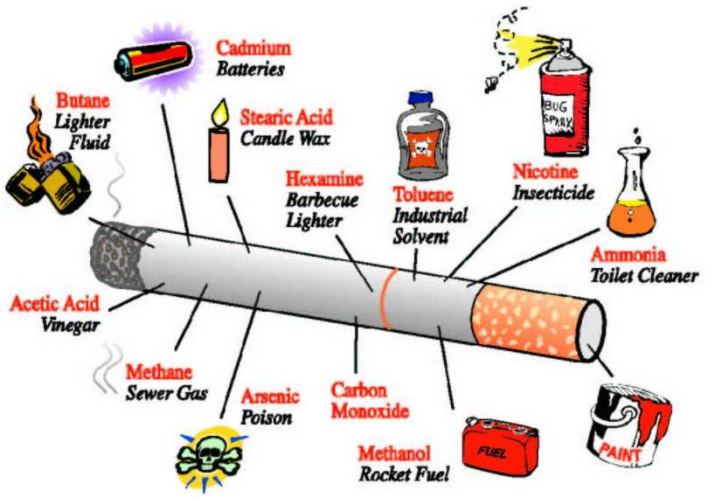
- Difficult to withdraw: 70% smokers intended to quit smoking → only 3% succeeded

- Some medications have been studied to be used for the treatment of nicotine addiction, and the methods widely used currently are nicotine replacement therapies (Berretini, 2005).

- Previous research:
  - The role of arachidonic acid pathway in drug dependent: Diclofenac as COX inhibitor decrease reward in rat nicotine addiction (Sjah, 2007)
  - Low dosage of diclofenac (1 mg/kg bw and 3,2 mg/kg bw) decreased EP receptor (Faridah, 2010; Anggraeny et al, 2012)

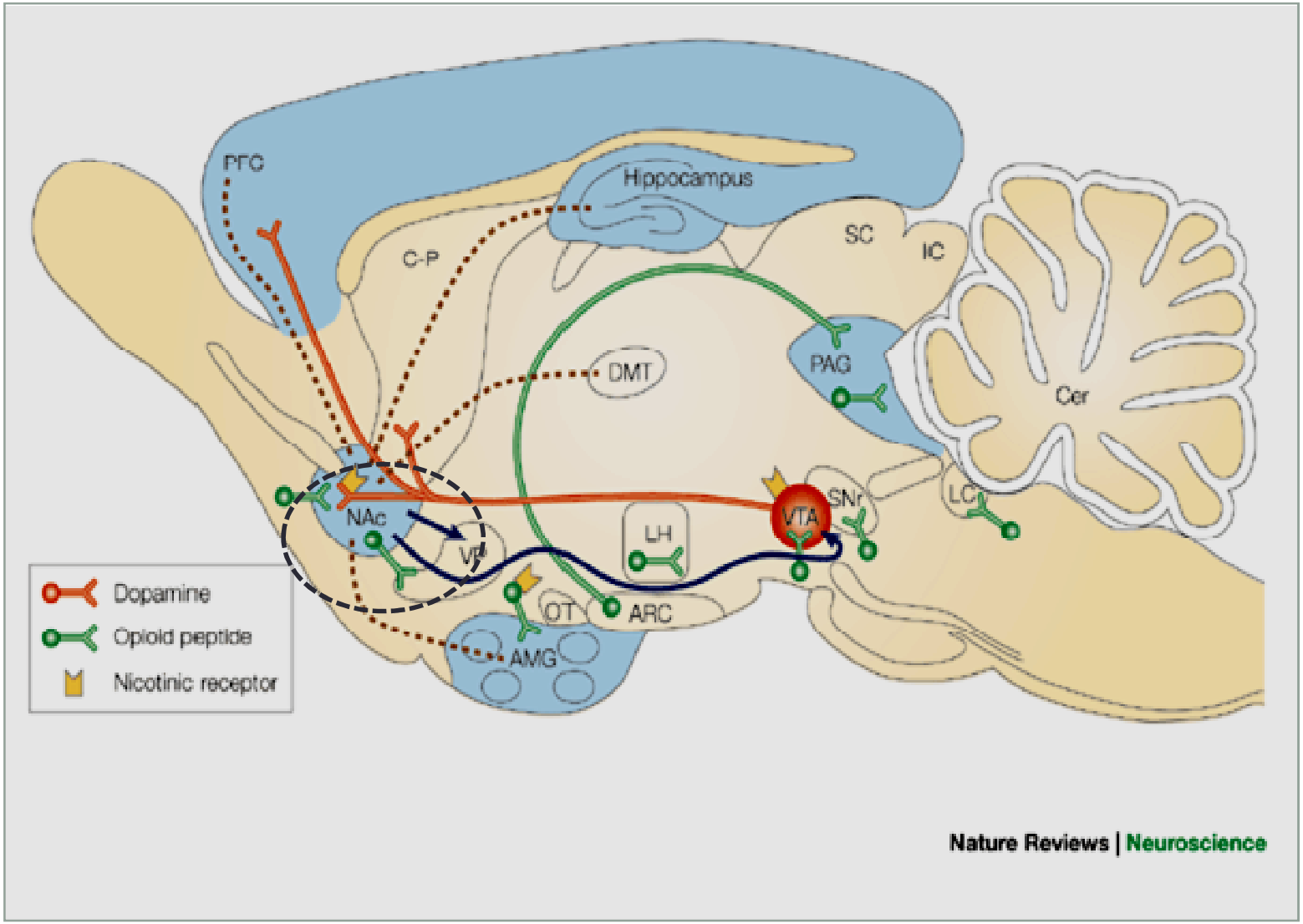
Nicotine and neurotransmitters





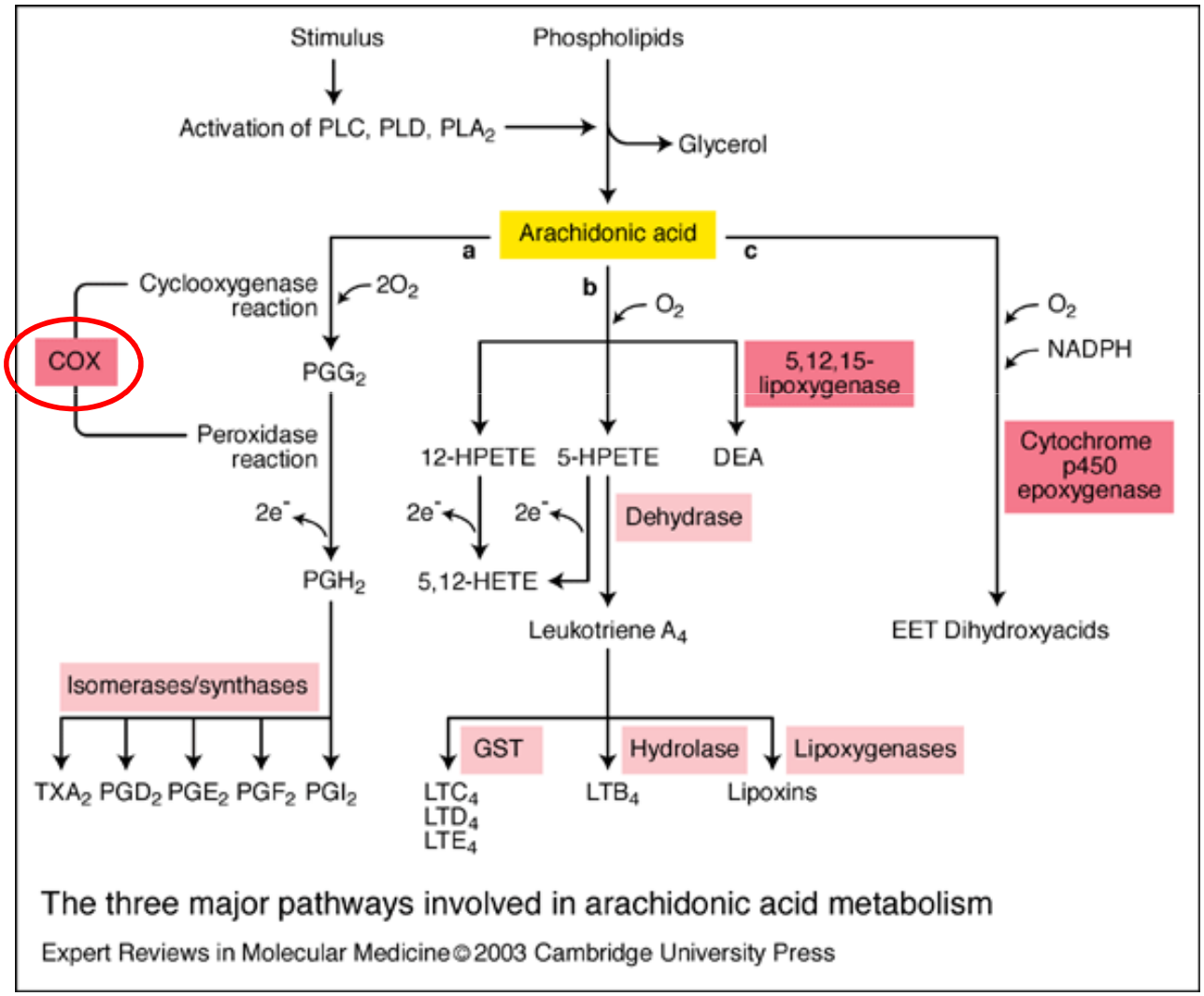
Benowitz,2008

Neuro-signaling in nicotine addiction



Nestler, 2001

Arachidonic acid pathway: drug addiction and inflammation pathway



The three major pathways involved in arachidonic acid metabolism

Background

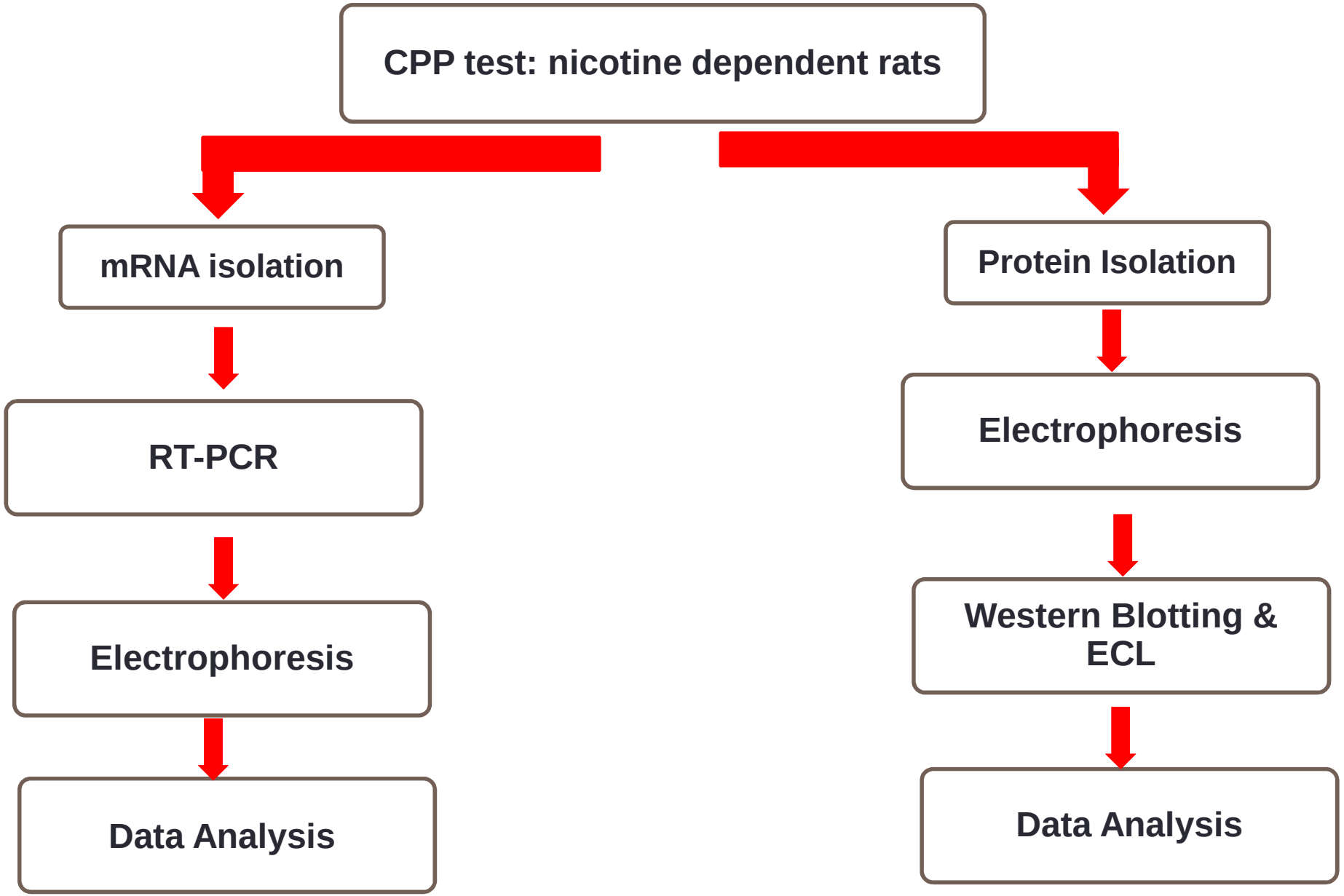
- GLUT-1 is one of glucose transporters that plays important role in brain glucose transport (Gerhart et al., 1989; Maher et al, 1994; Kumagai et al., 1994)
- Chronic use of addictive substance influences the rate of metabolism in the brain, especially glucose metabolism (Volkow et al., 1997)
- Drug dependence and withdrawal changed brain glucose metabolism (Volkow et al., 1991)

GLUT-1 has important role in drug addiction

Aim of the research

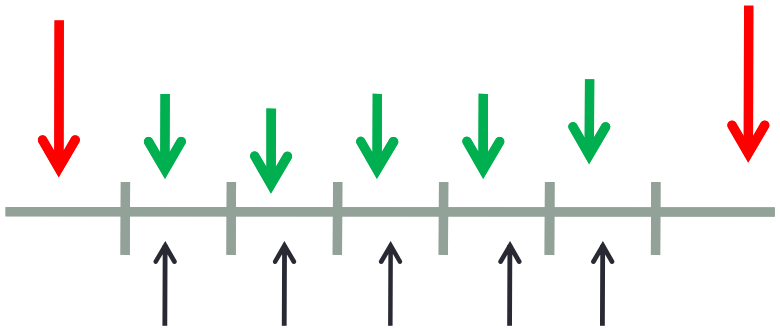
- To study the expression of GLUT-1 receptor in nicotine dependent rat brain
- To study the effect of diclofenac as *Non Steroidal Anti Inflammatory Drugs* (NSAID) in GLUT-1 receptor expression

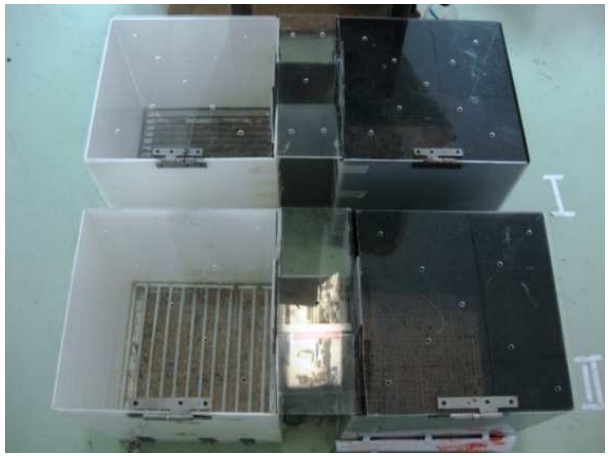
Research methodology



Outline for CPP test

- Nicotine 0.5 mg/kg 1x/hari i.p
- *Preference test (CPP)*

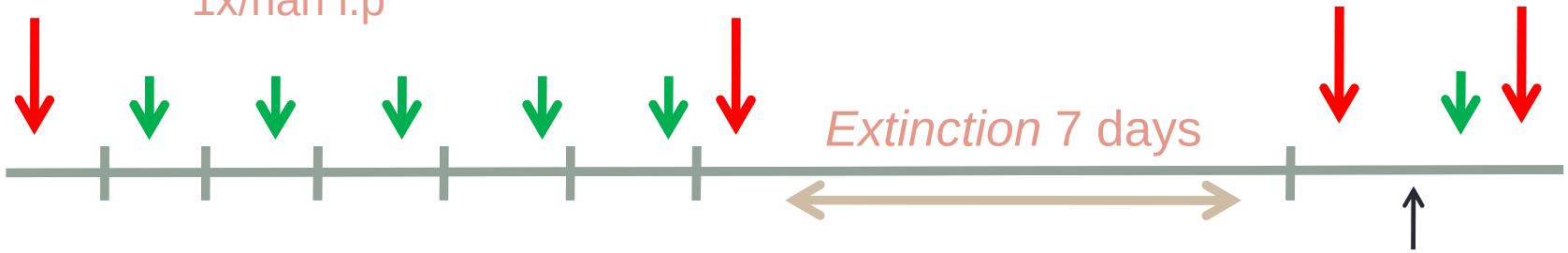




- Diclofenac 3.2 mg/kg i.p

Sebelum induksi nikotin

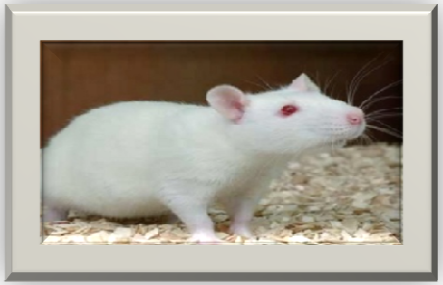
- Nicotine 0.5 mg/kg 1x/hari i.p
- *Preference test (CPP)*



- Diclofenac 3,2 mg/kg i.p

Before nicotine induction

Research design



Rat habituation

Pre conditioning

Dependence group

Post Conditioning

Organ isolation(mRNA & Protein)

Spectrophotometry

PCR

WB

Dependence group

Conditioning with nicotine

Conditioning with nicotine & Diclofenac

Organ isolation (mRNA & Protein)

Spectrophotometry

PCR

WB

Relapse group

Conditioning with nicotine

Post Conditioning

Extinction

Relapse with nicotine

Relapse with nicotine & Diclofenac

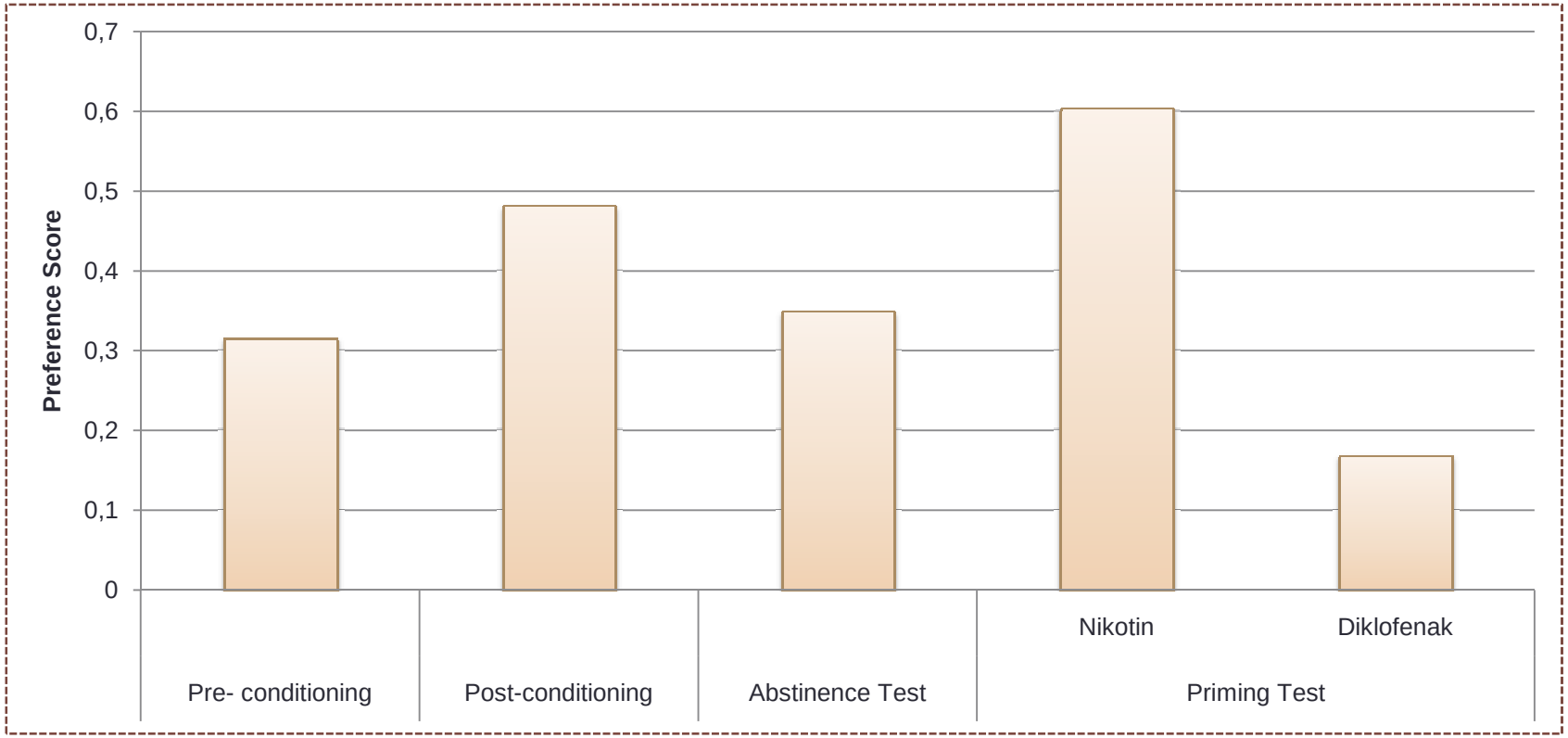
Organ isolation(mRNA & Protein)

Spectrophotometry

PCR

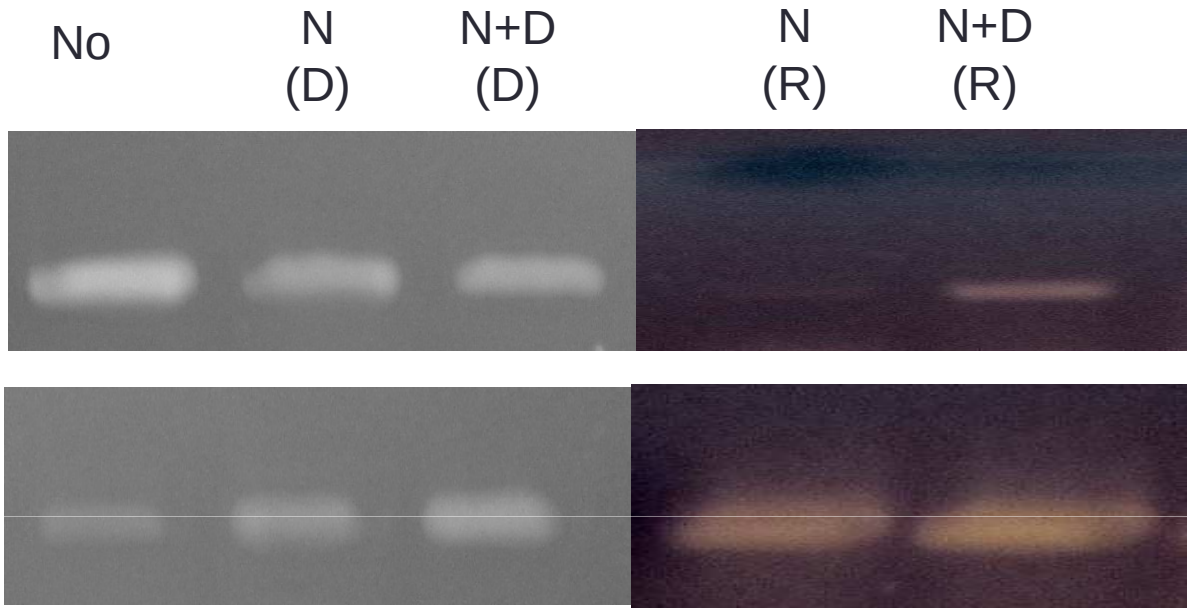
WB

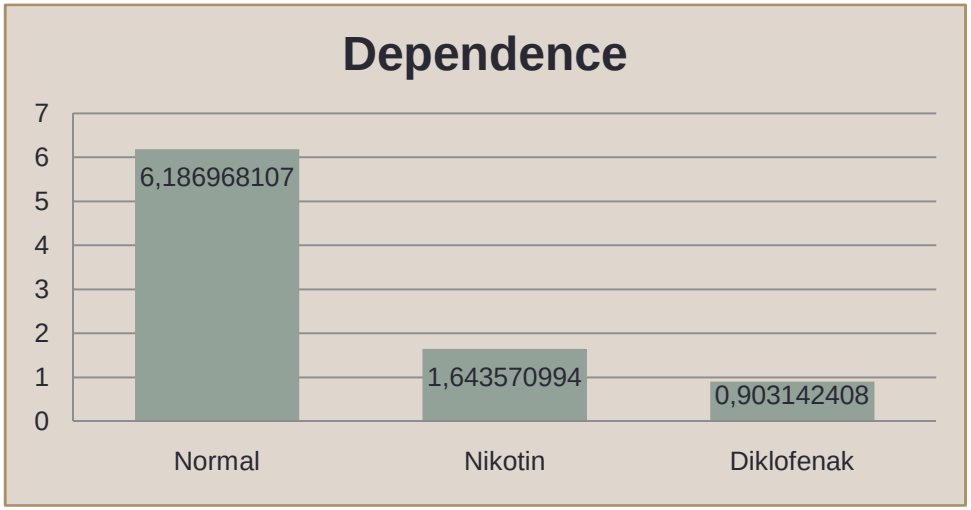
CPP Results

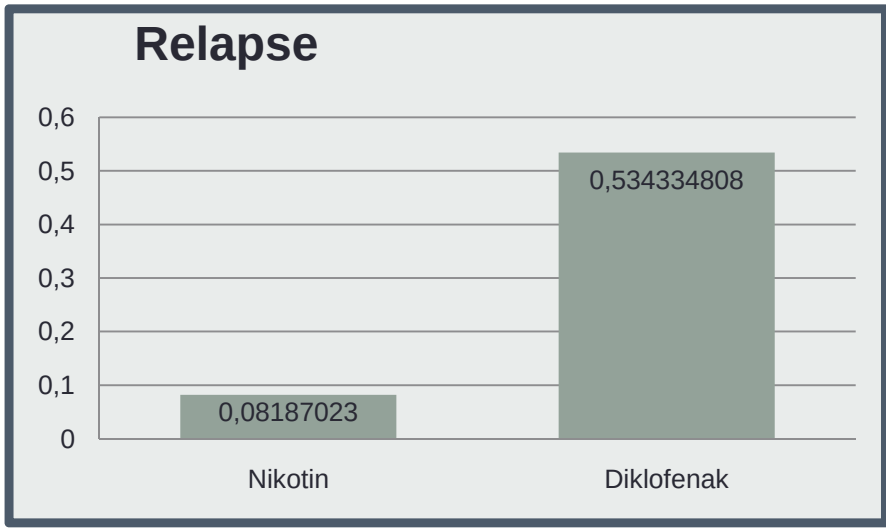


Based on CPP test, nicotine induced dependency in rats, and diclofenac reduced nicotine dependency.

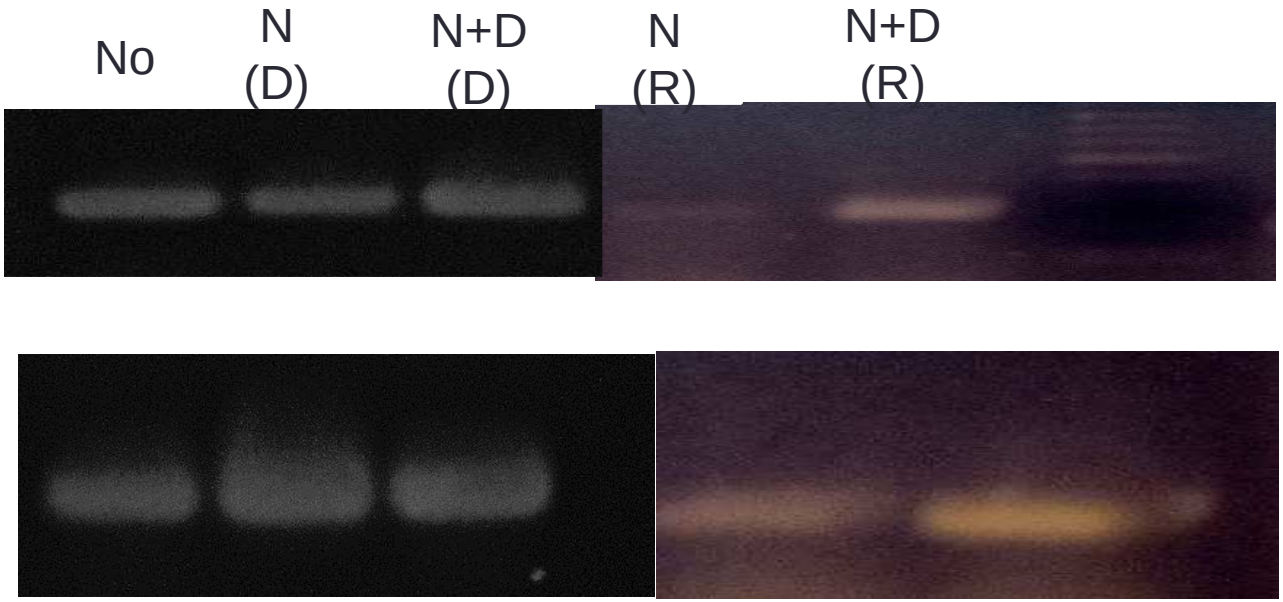
Expression level of GLUT-1 mRNA in Hipocampus

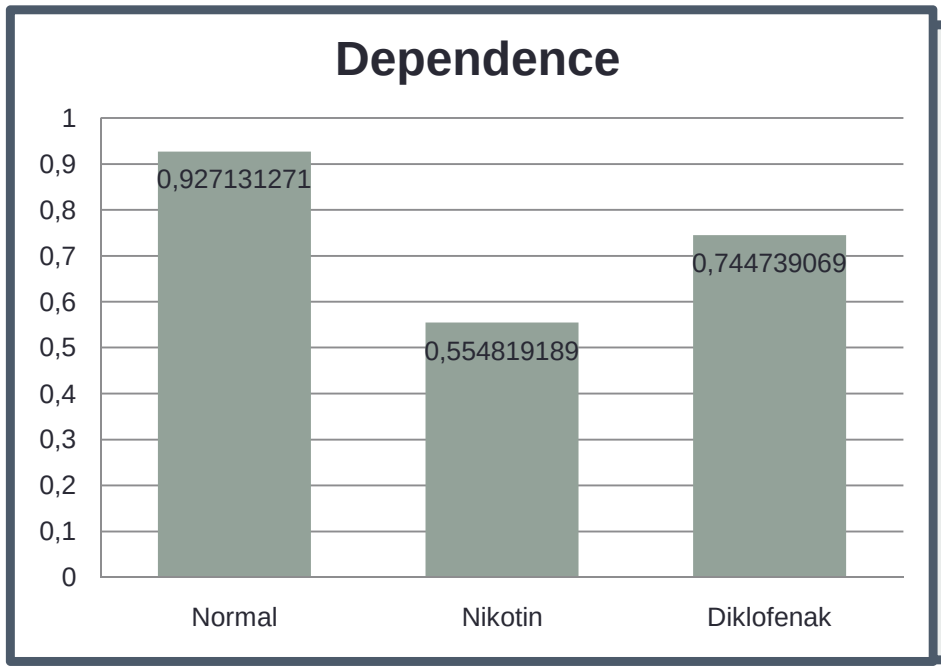


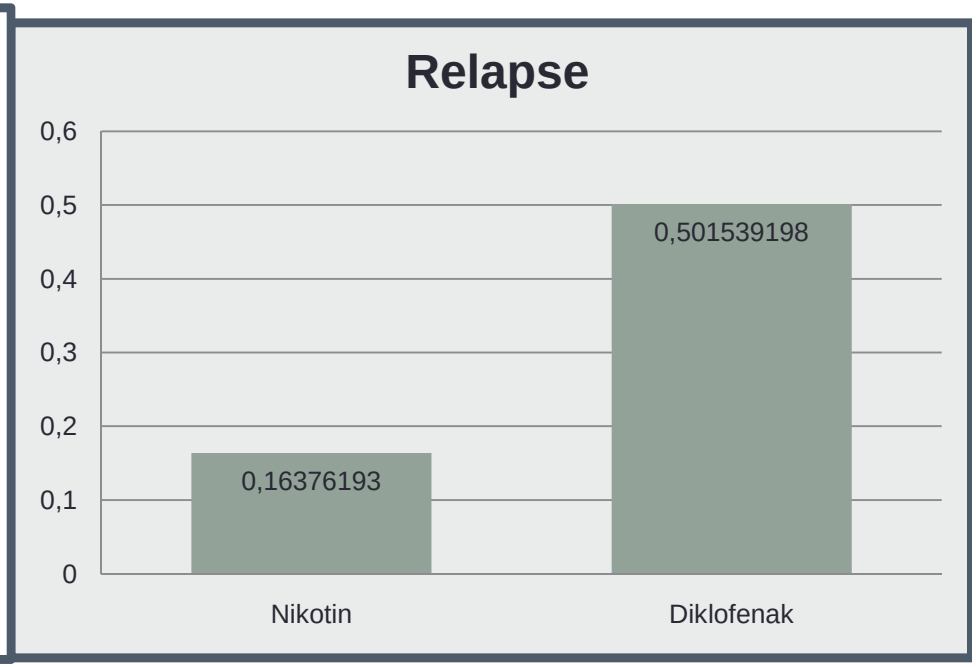




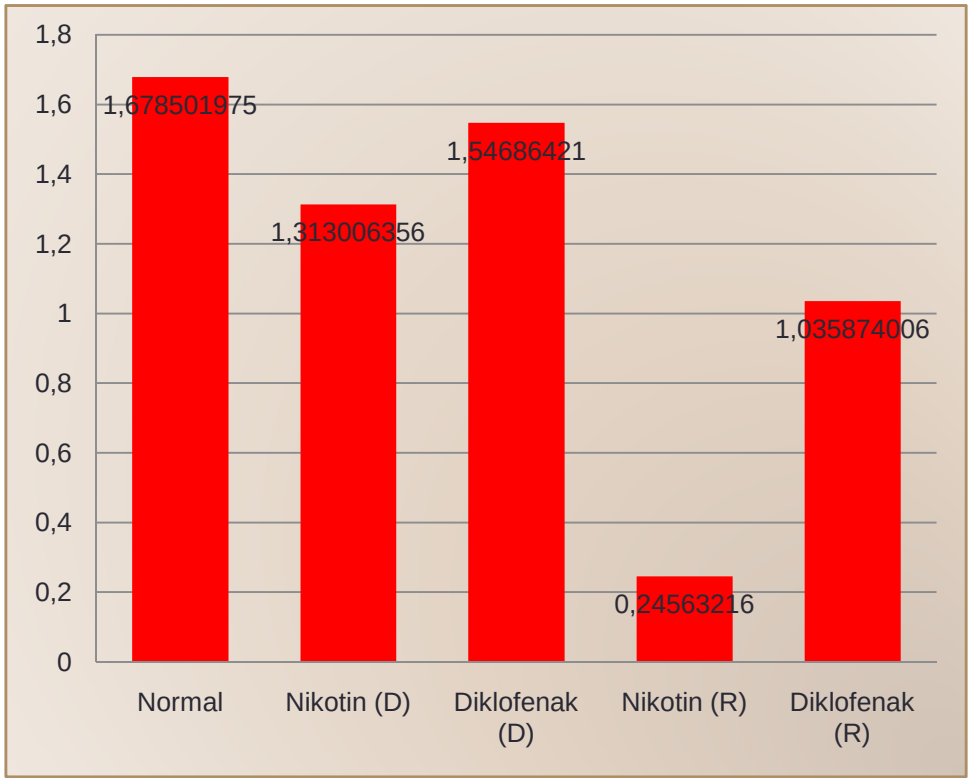
Expression level of GLUT-1 mRNA in Bulbus



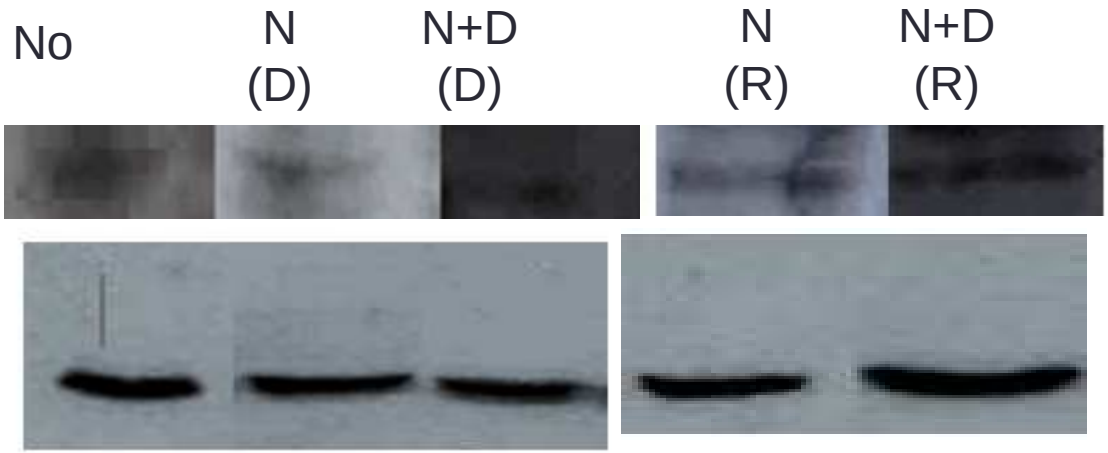


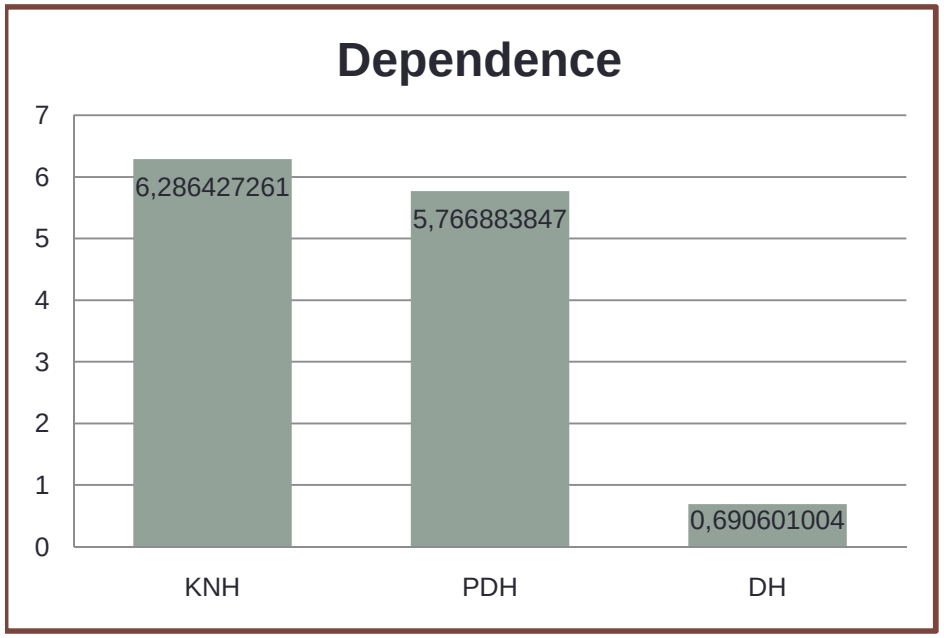


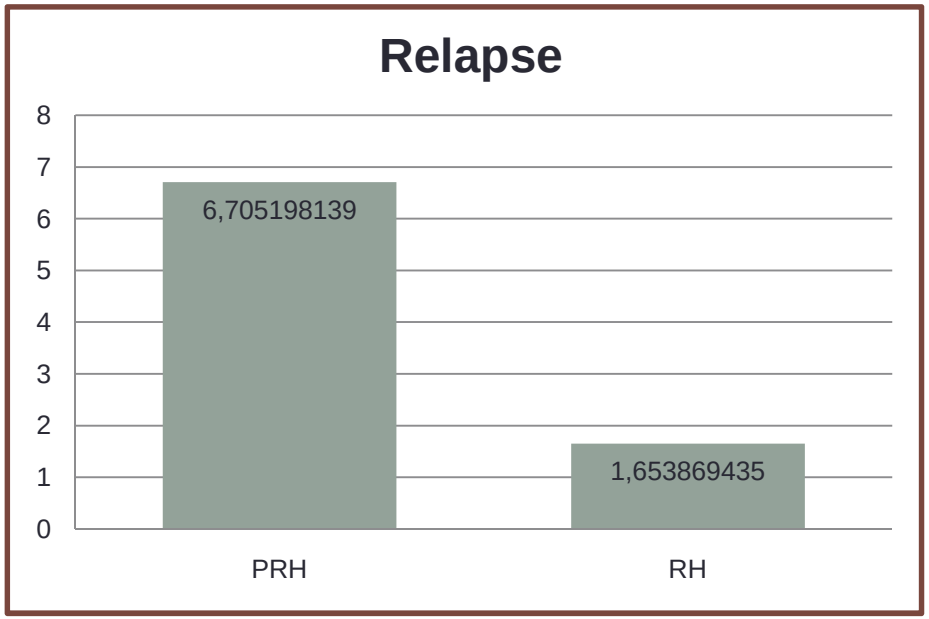
Expression level of GLUT-1 mRNA



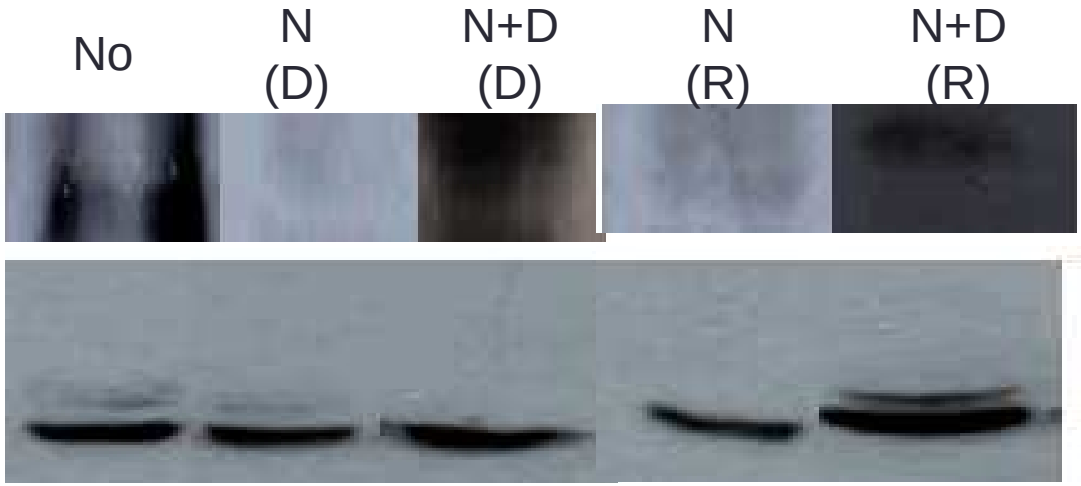
Expression level of GLUT-1 receptor in Hipocampus

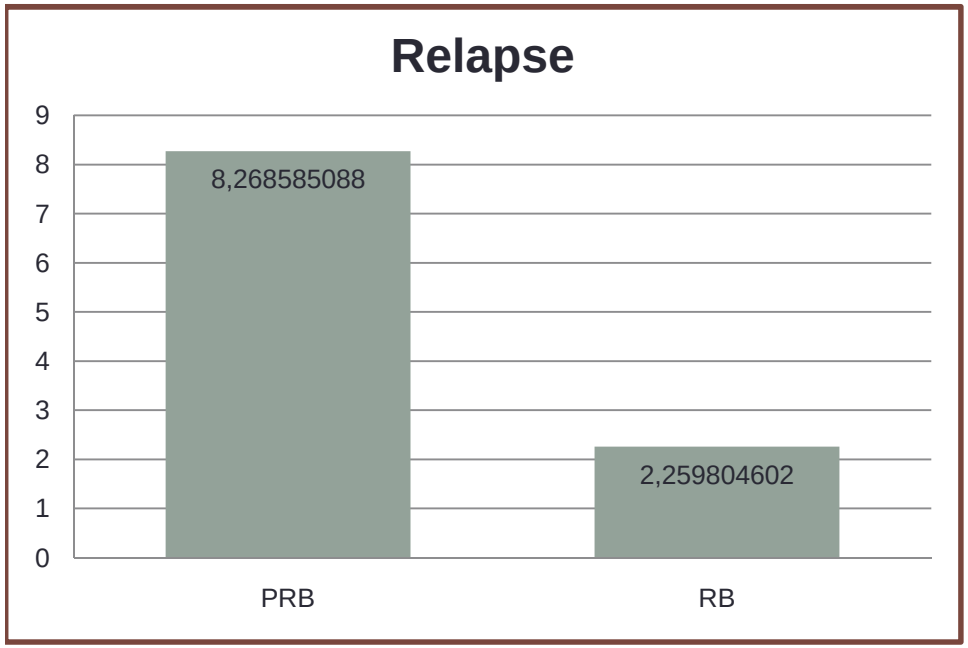


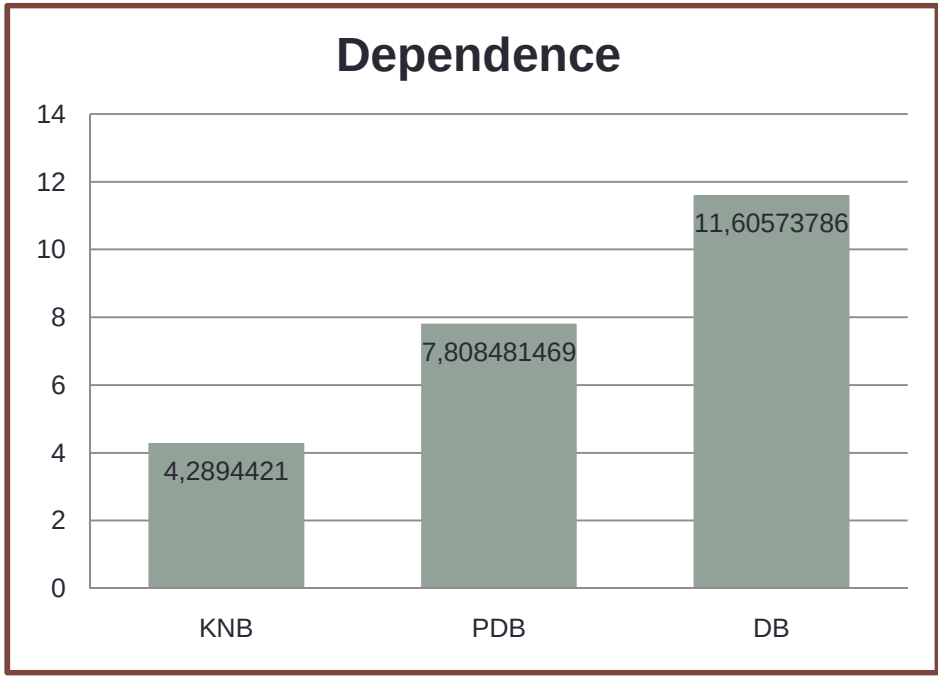




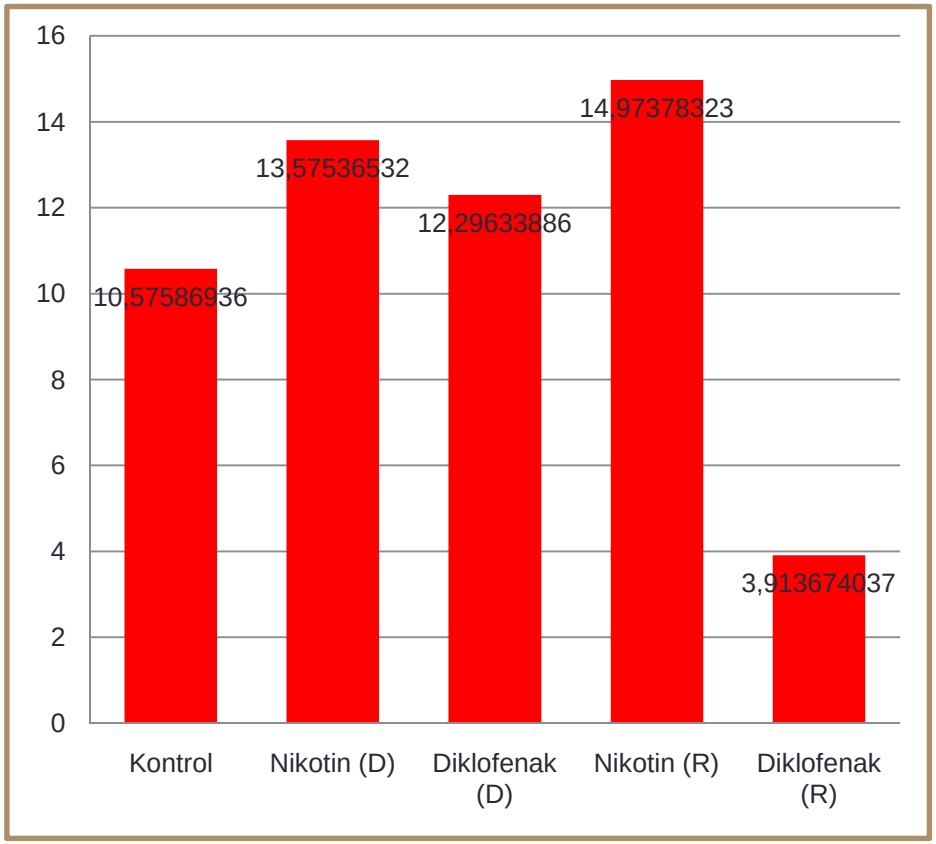
Expression level GLUT-1 receptor in bulbus

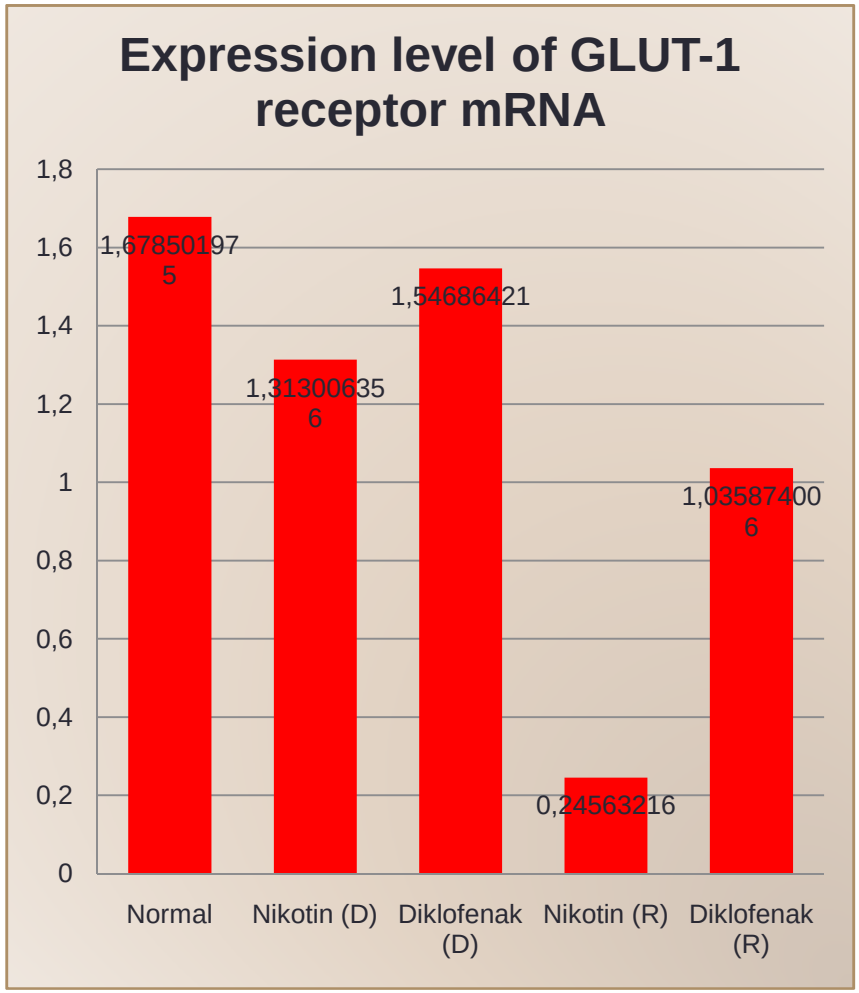


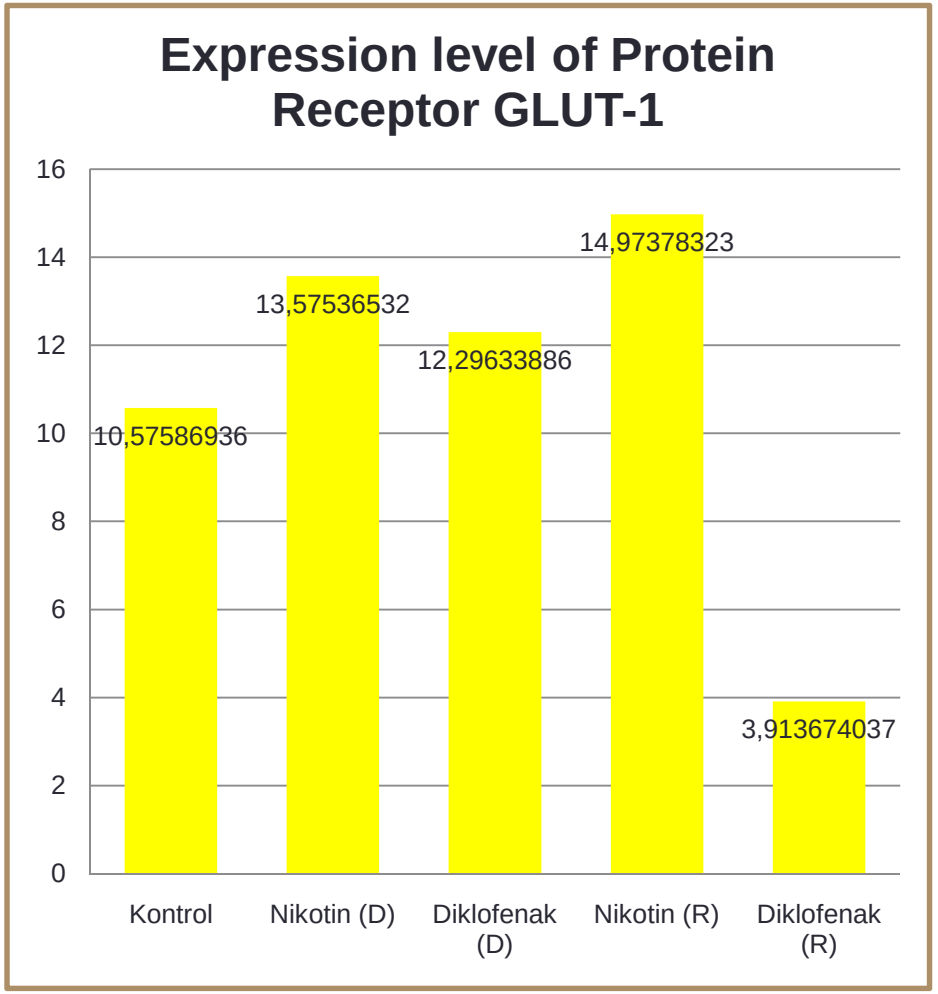




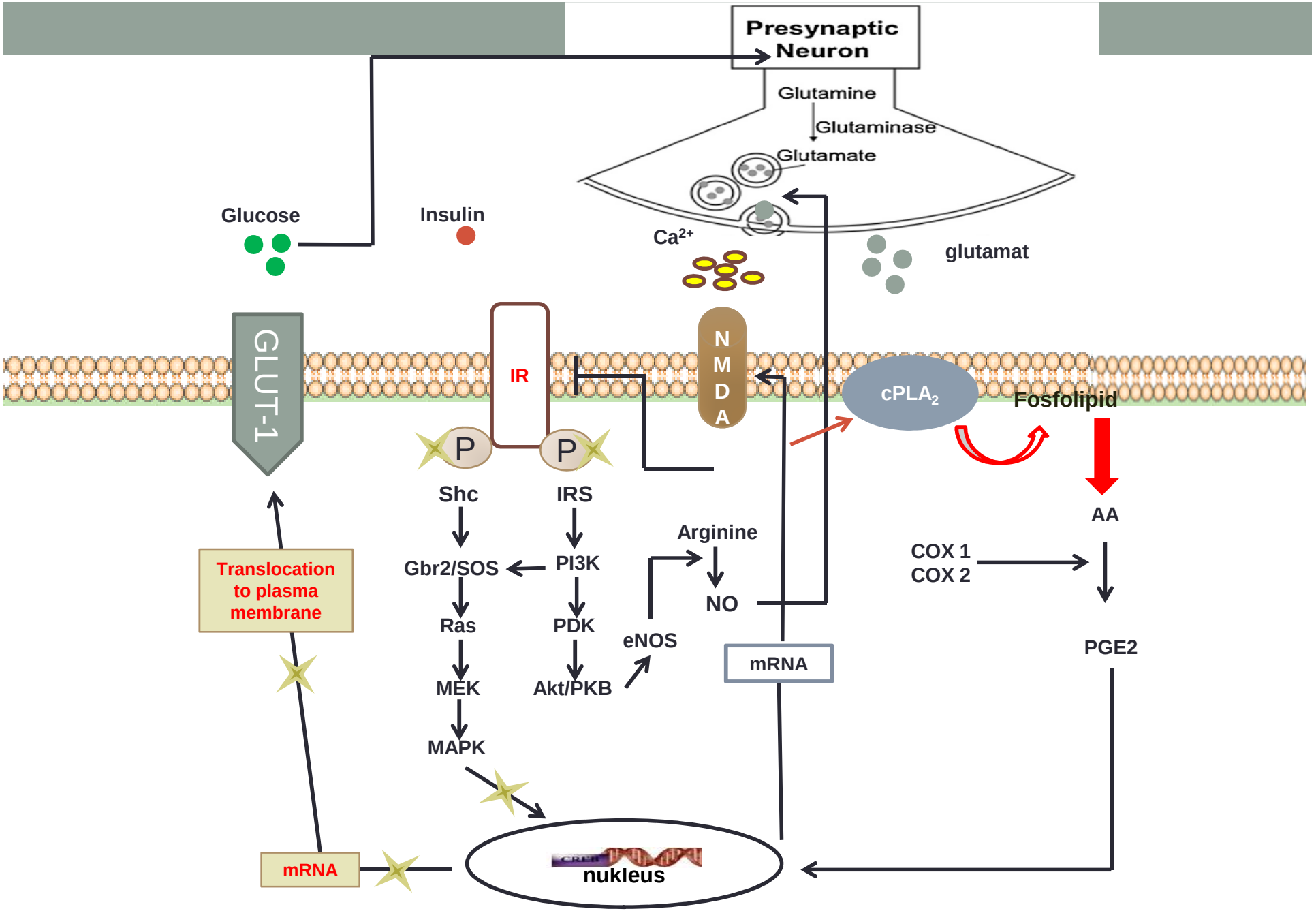
Expression level of GLUT-1 receptor



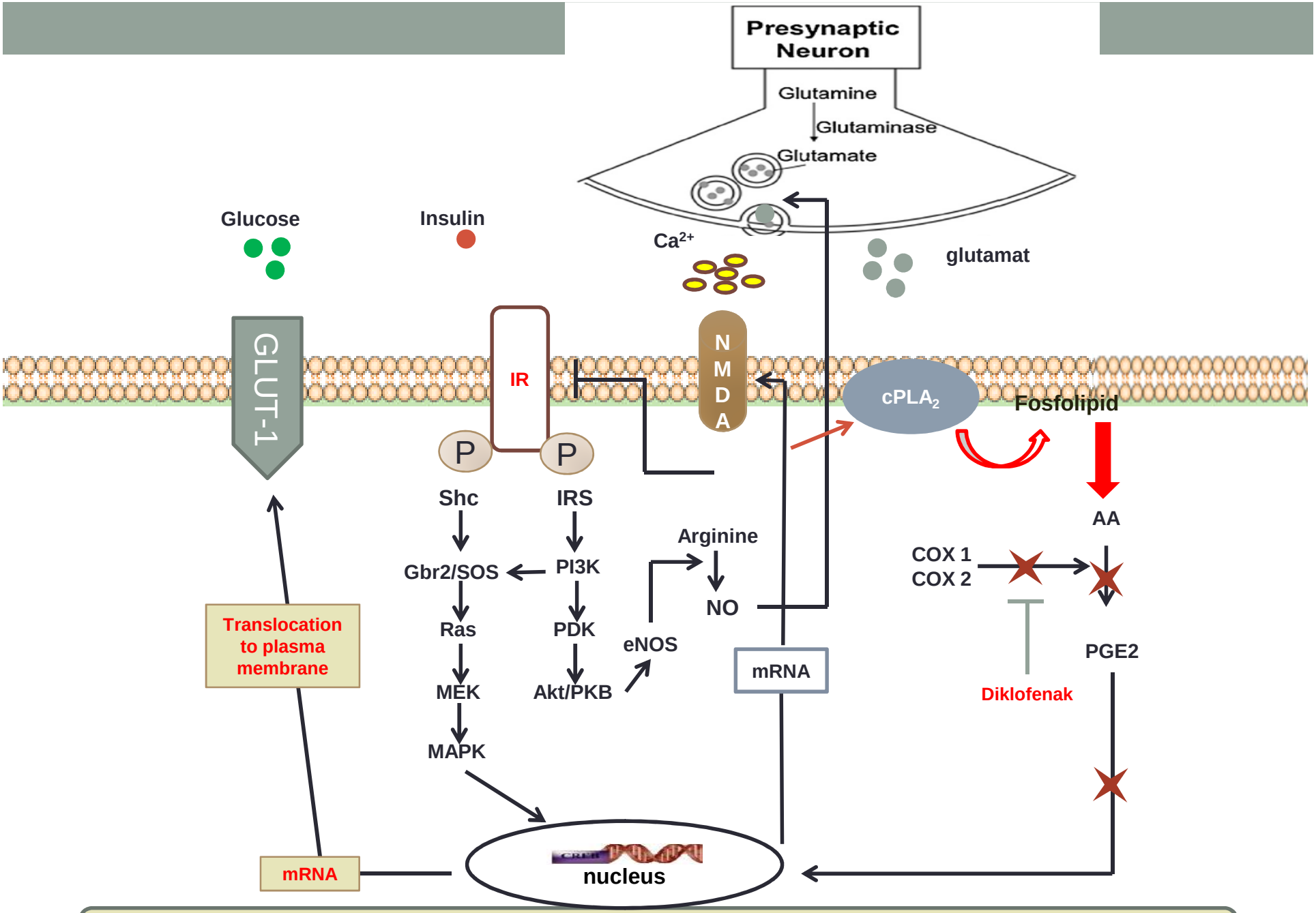




Post-transcriptional modification: nicotine dependent (D/R) GLUT-1 receptor increased, diclofenac (D/R) decreased GLUT-1 receptor



POSSIBLE MECHANISM OF NICOTINE-DEPENDENT AND GLUT-1 RECEPTOR EXPRESSION, AND DICLOFENAC IN AA PATHWAY AS ANTI-ADDICTION DRUG



POSSIBLE MECHANISM OF NICOTINE-DEPENDENT AND GLUT-1 RECEPTOR EXPRESSION, AND DICLOFENAC IN AA PATHWAY AS ANTI-ADDICTION DRUG

Conclusion

- Nicotine reduced GLUT-1 receptor in mRNA level
- Diclofenac (3,2 mg) treatment increased GLUT-1 receptor in mRNA level
- There is post-transcriptional modification → in nicotine dependent rat brain GLUT-1 receptor in protein level increased
- Diclofenac (3,2 mg) treatment decreased GLUT-1 receptor in protein level