

**OPIOIDE
ENDOGENO**

RECEPTOR

**DENOMINACION
MOLECULAR**

**Beta-endorfinas
Endomorfina**

μ

MOR

Encefalinas

δ

DOR

Dinorfinas

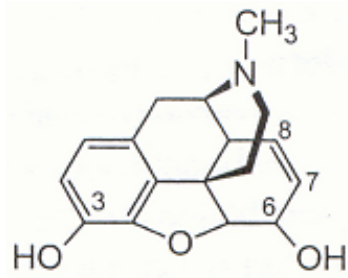
κ

KOR

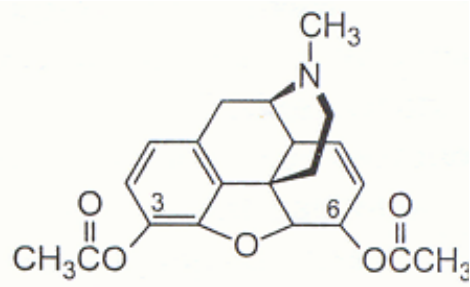
Orfanina

-

ORL-1



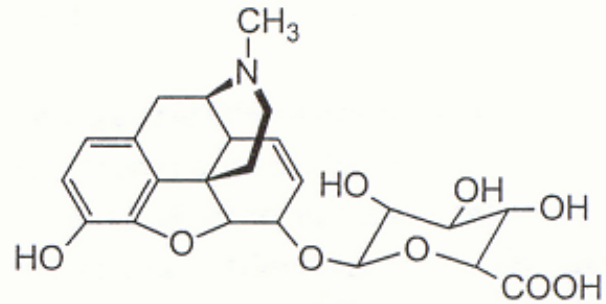
Morphine



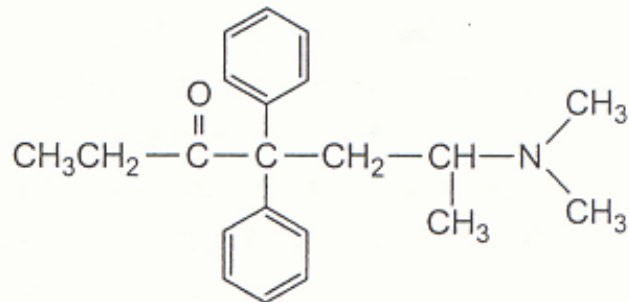
Heroin



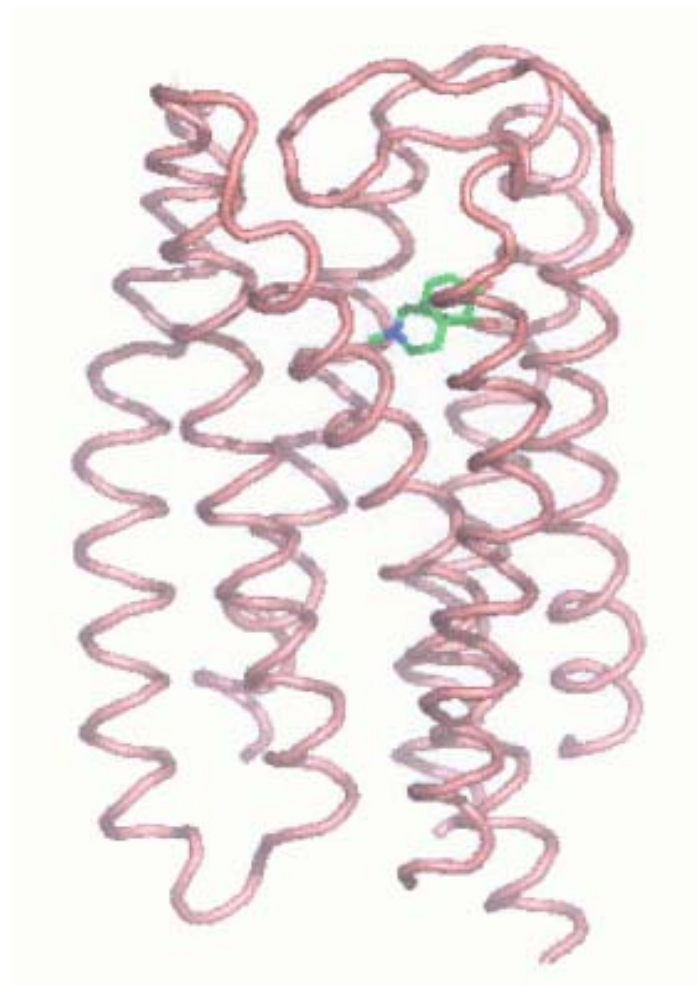
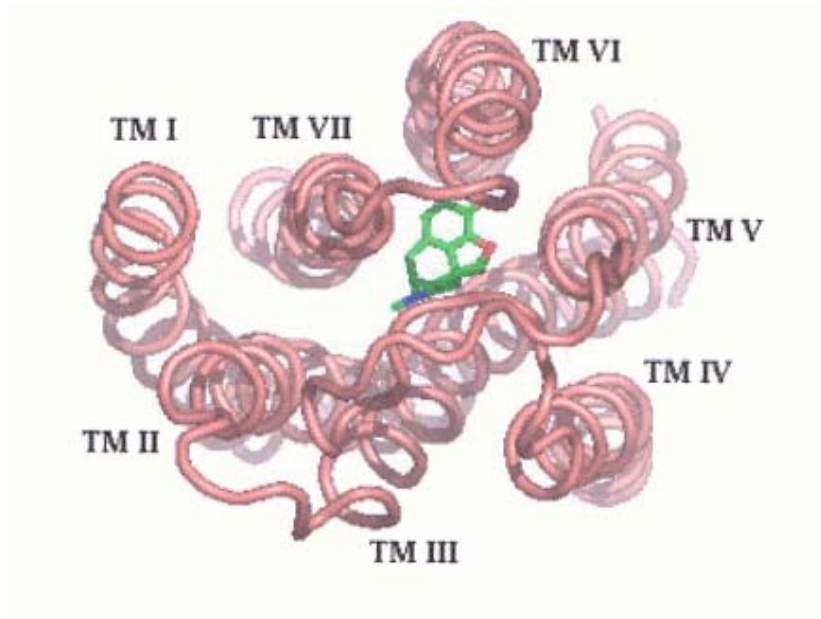
Fentanyl



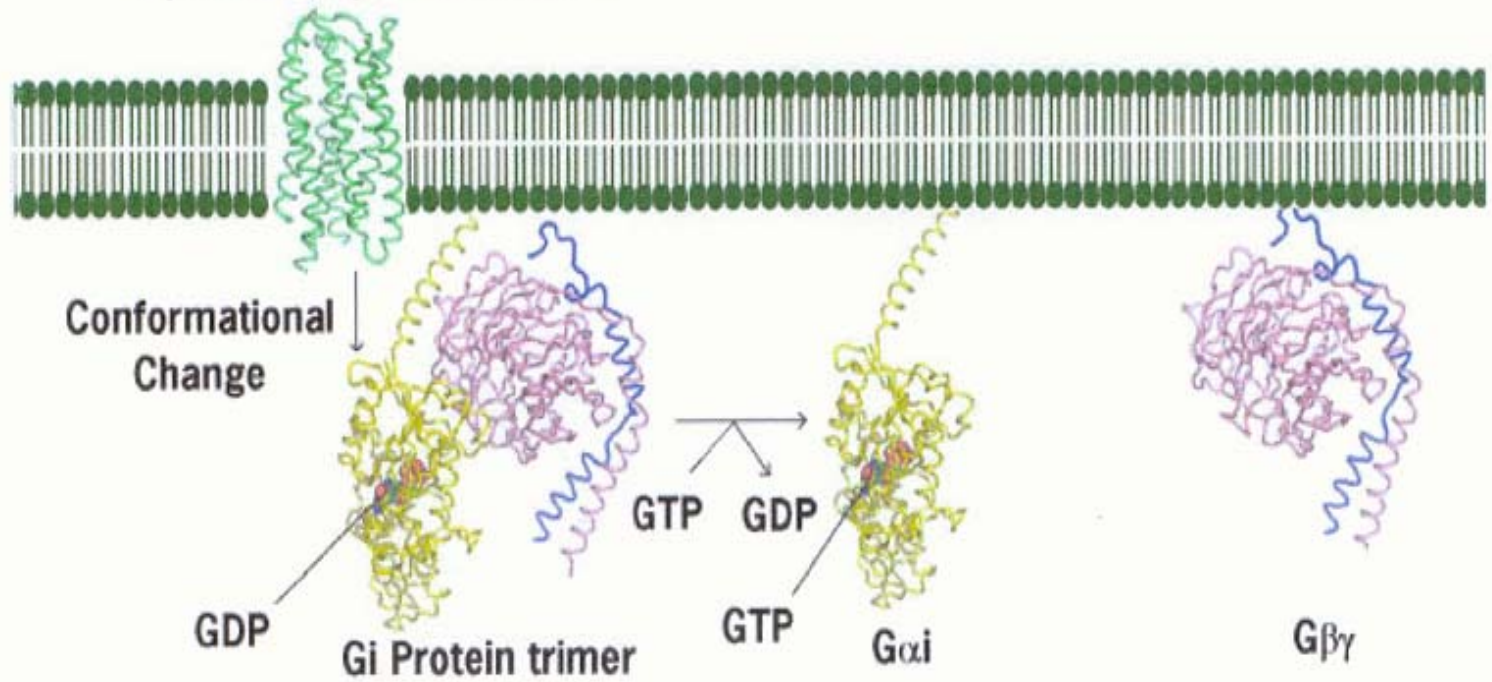
Morphine-6β-glucuronide



Methadone

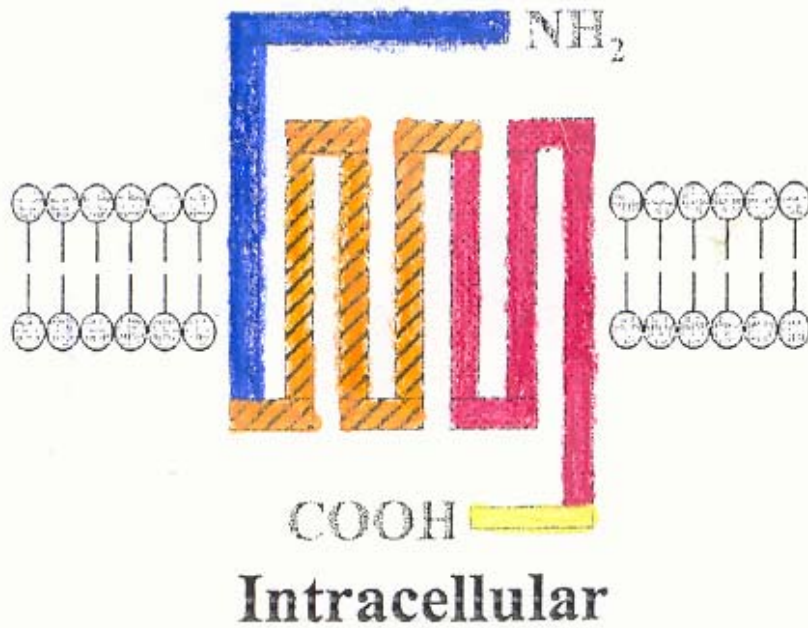


Opioid Receptor Activation

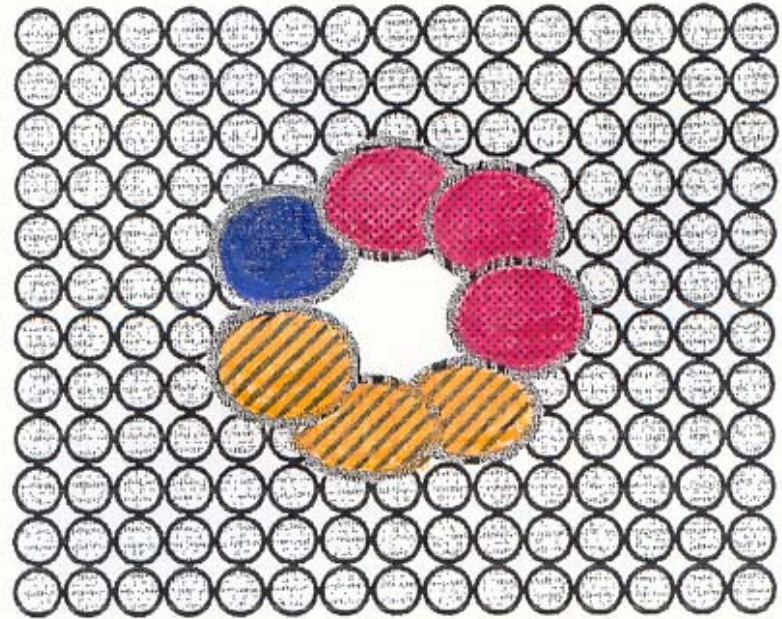


Side

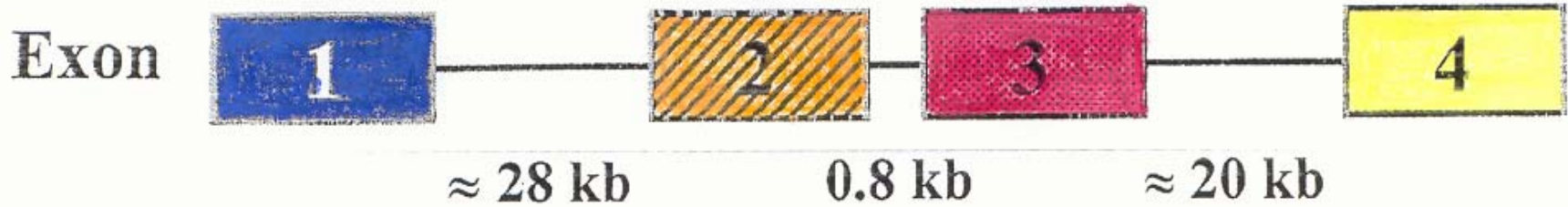
Extracellular



Surface

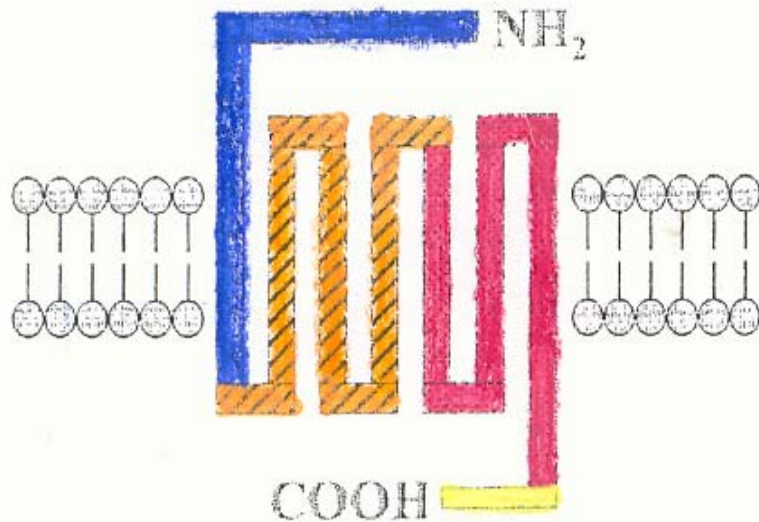


MOR-1



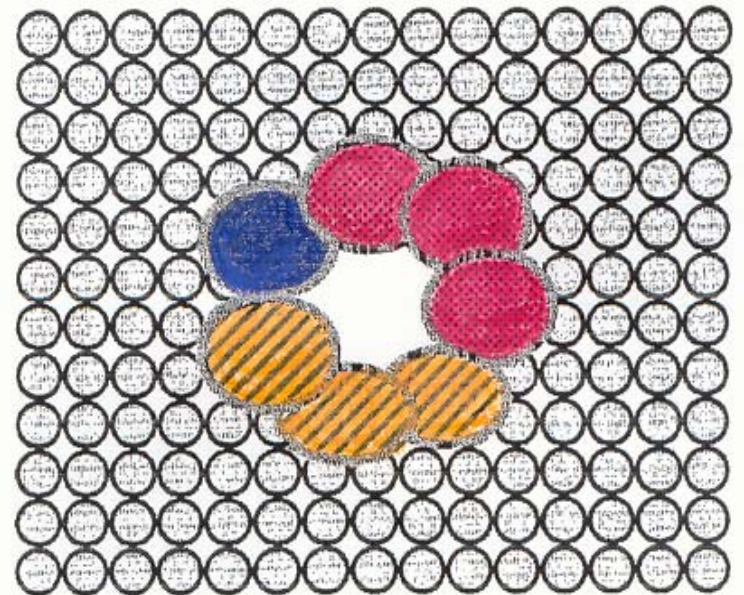
Side

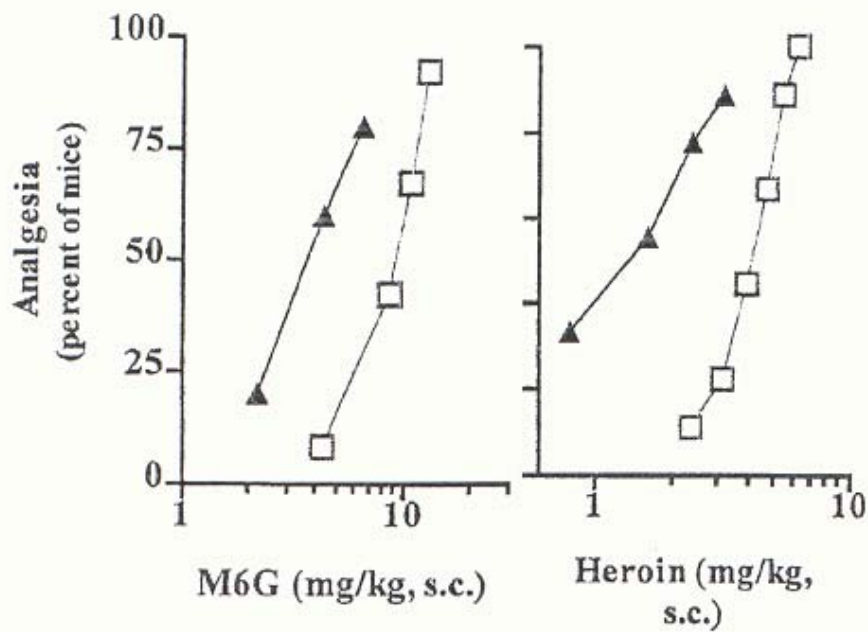
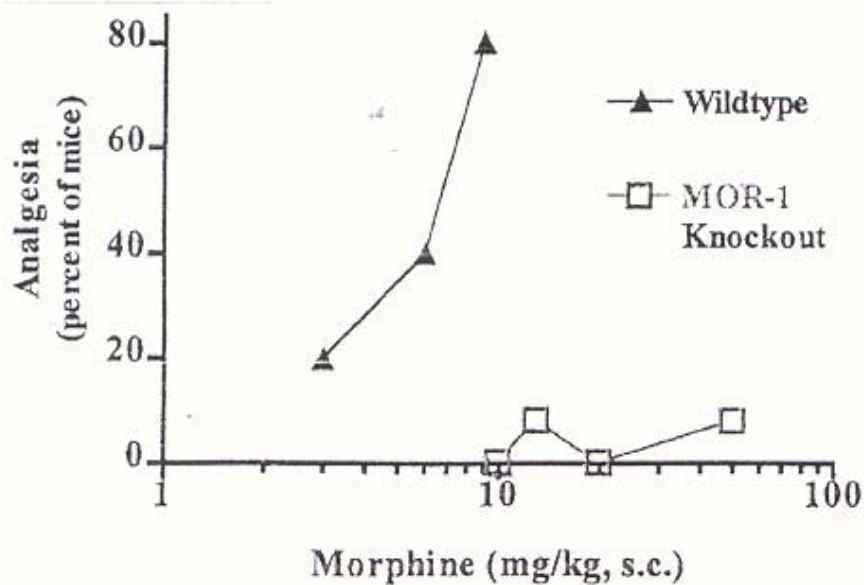
Extracellular



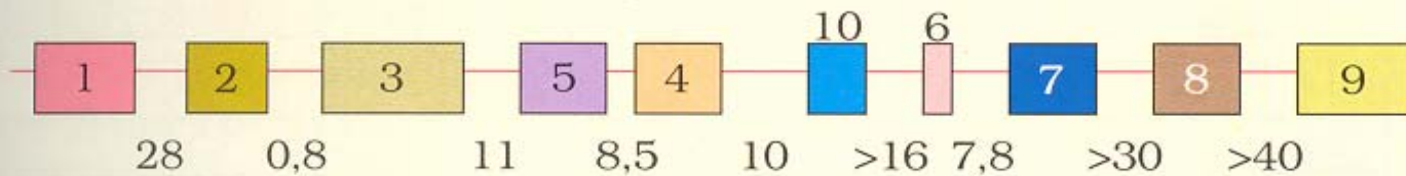
Intracellular

Surface



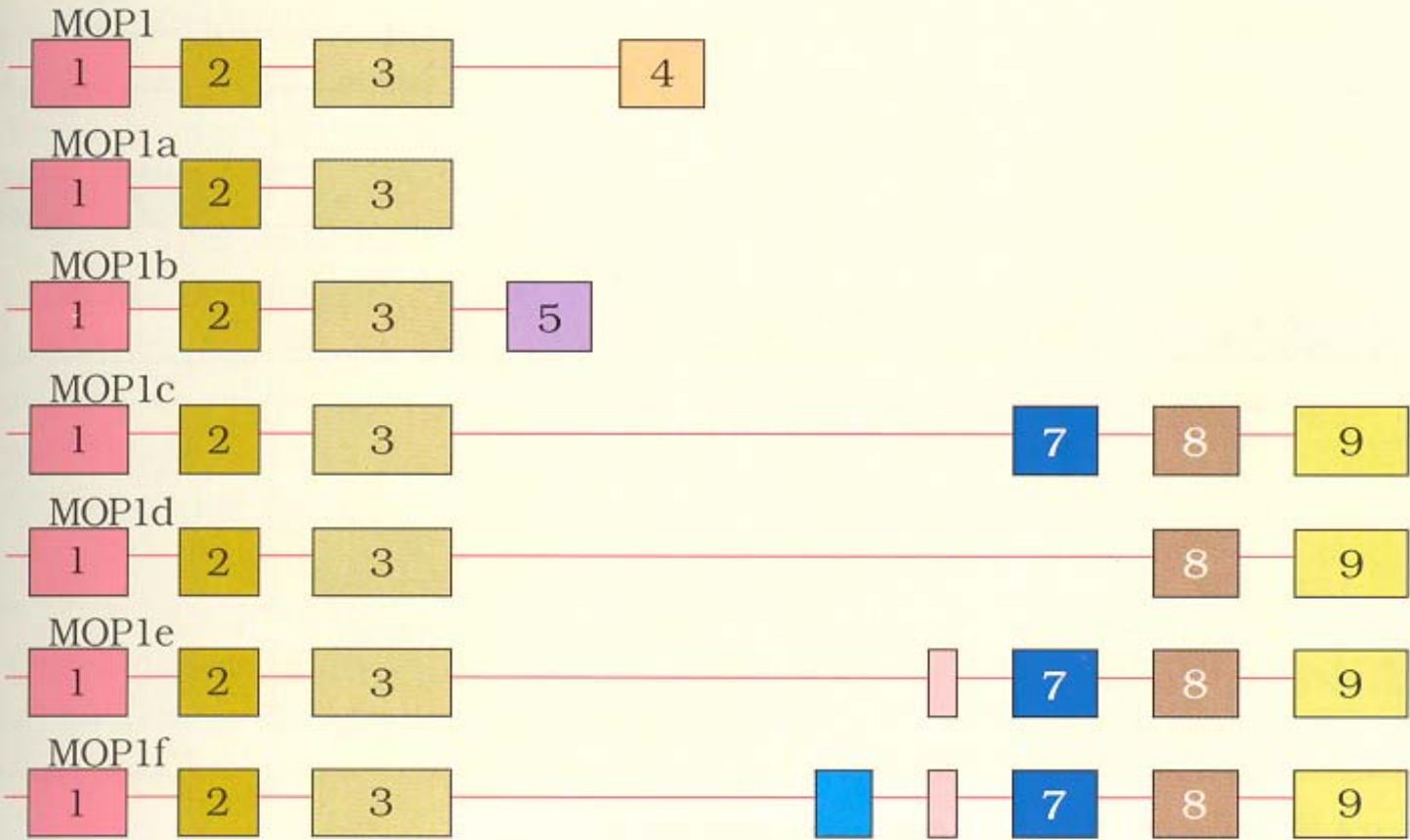


Exón



Intrón (kb)

Variantes de splicing



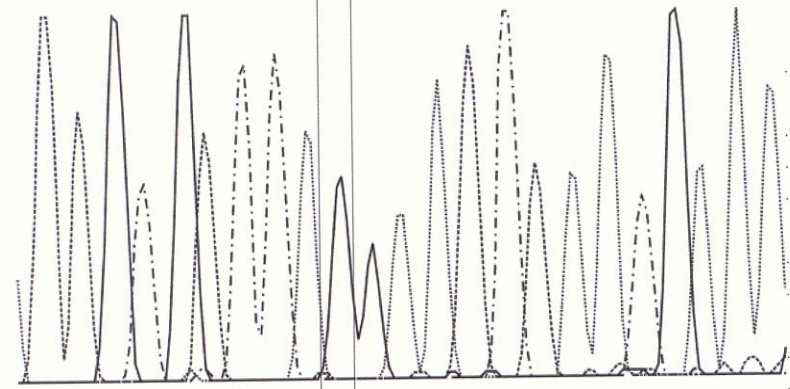
118

cDNA

TTAGATGGCAACCTGTCCGACCC

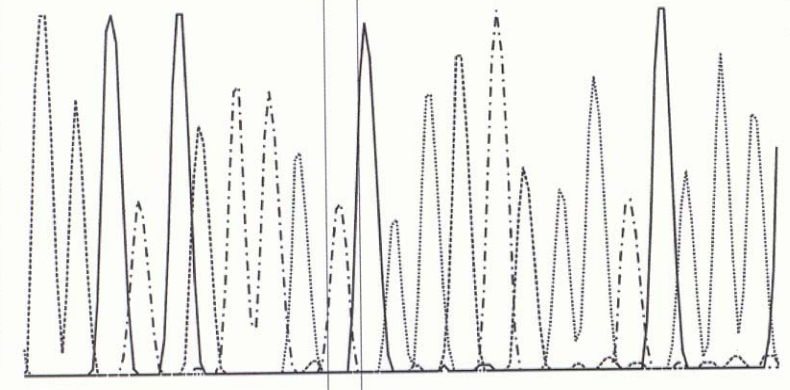
Patient B: A118/A118

TTAGATGGCAACCTGTCCGACCC



Patient S: G118/G118

TTAGATGGCGACCTGTCCGACCC



DOSIS OPIOIDE

INTENSIDAD

DOLOR

+

TOLERANCIA

TOLERANCIA A OPIOIDES

- Desacoplamiento receptor μ -proteína G
- Desensibilización receptor μ
- Infraregulación receptor μ
- Supreregulación adenilciclasa
- Proteína Gs (gangliósido GM1)
- Producción neuropéptidos endógenos
- Activación NMDA
- Apoptosis neuronas inhibitorias

OPIOIDE



RECEPTOR



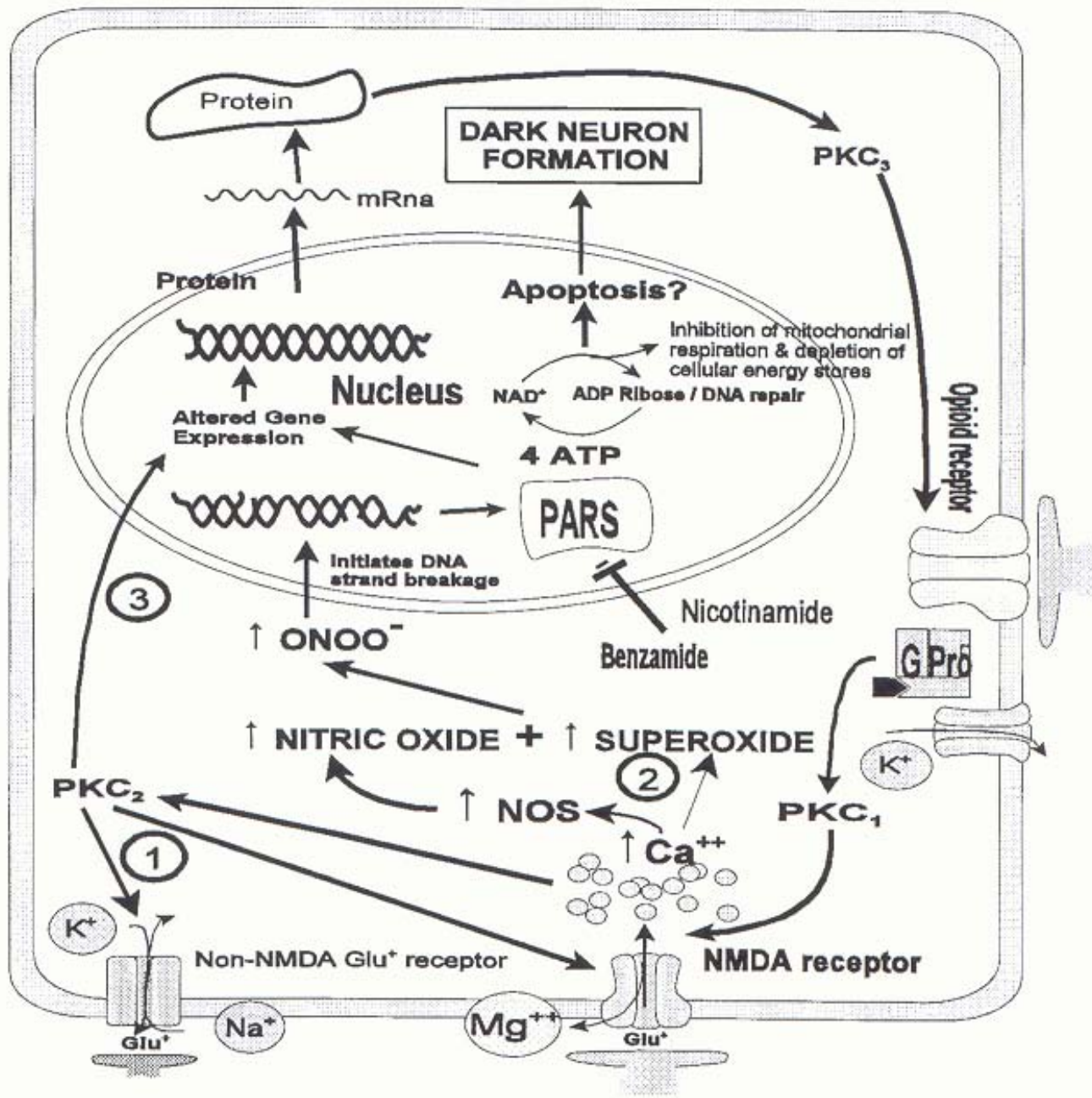
GM1

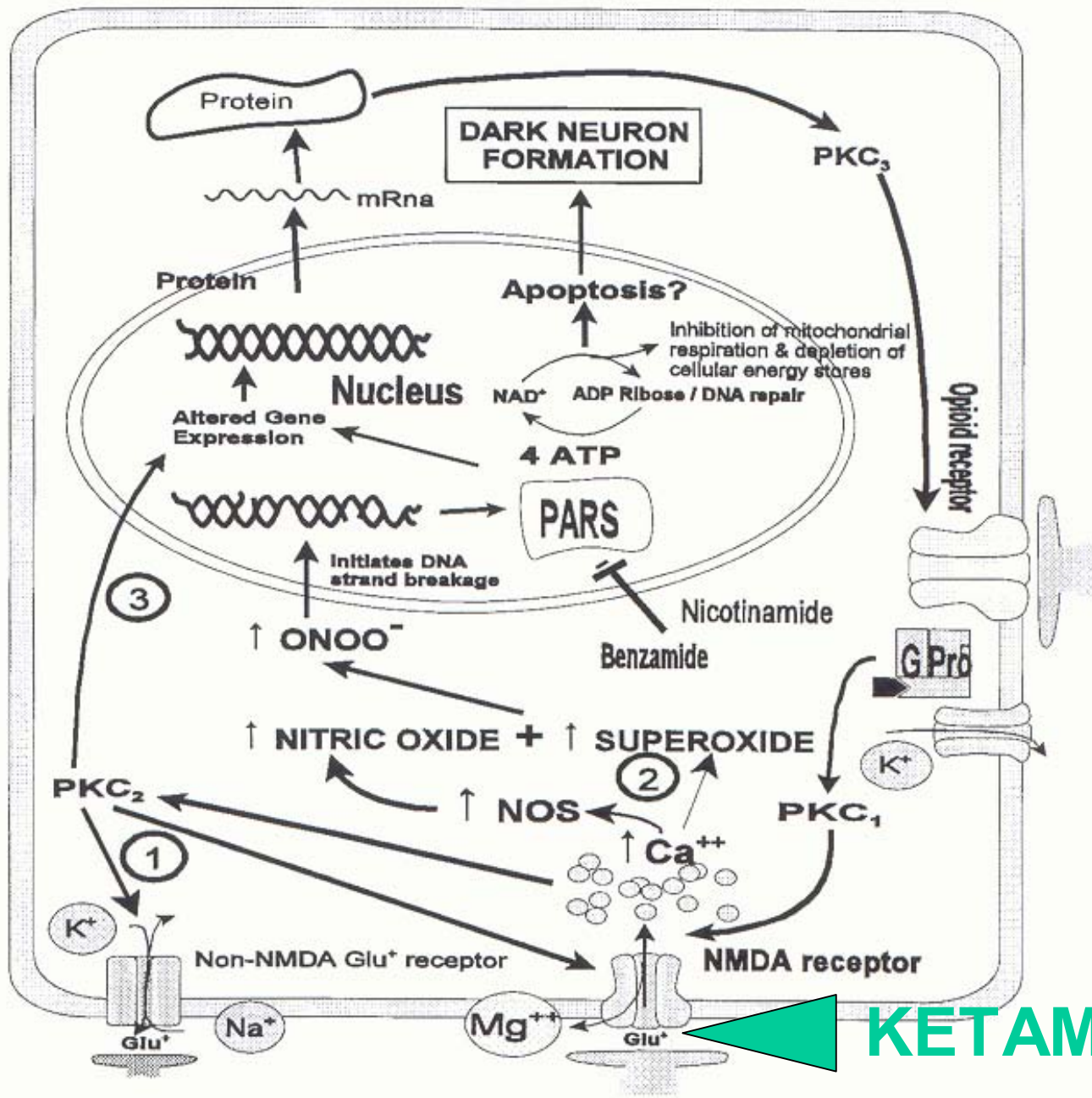
Gi INHIBICION
ANALGESIA

Gs EXCITACIÓN
TOLERANCIA
HIPERALGESIA
NEUROTOXICIDAD?

Naloxona







KETAMINA

0

10

No dolor

X
Máximo dolor
imaginable

PACIENTE 1

PACIENTE 2

Nocicepción

65%

20%

Somatización

5%

25%

D. Química

0%

35%

Incidental

25%

5%

Tolerancia

5%

15%

FACTORES QUE INFLUYEN EN ANALGESIA?

- Variantes splicing

Receptor μ

- Polimorfismos nucleótidos

- Polimorfismos MDR1
 MRP2

- Alteraciones CYP 450

