# G-Protein Receptors

External Signal
First Messenger (NT)

↓

Receptor

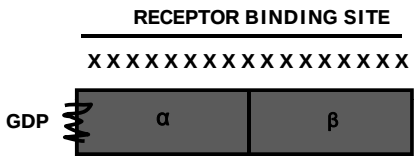
Transducer | Primary Effector

↓

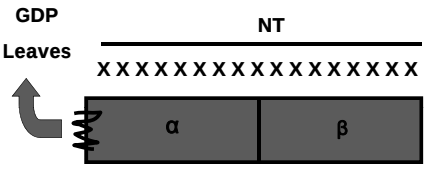
Second Messenger
Secondary Effector

- G Proteins

At Rest




- Stimulation begins

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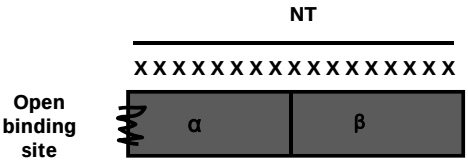
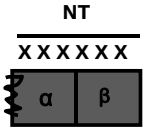
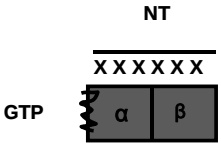


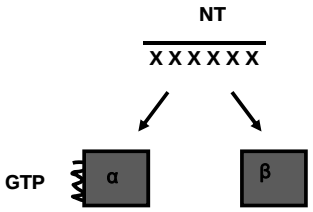

- Stimulation
- NT causes a conformational change and knocks off GDP
- Result- Leaves Alpha binding site open



- GTP binds to the open binding site.




- Causes a conformational change
- Get Dissociation

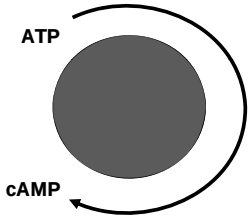



## Note

- GTP is converted by GTPase and ATP to GDP
- Causes Alpha and Beta subunits to bind together and link to the receptor site

## Adenylyl Cyclase (AC)

- When activated makes cAMP from ATP
- cAMP is an intracellular messenger

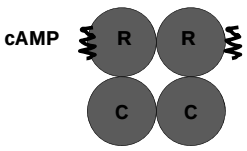



## Kinases

- Kinases put phosphate groups on something.
- Where: A protein (Ion Channel)
- Result: Protein Kinase
- Many types of PK
  - CAMP Protein Kinase
  - CaCal Protein Kinase
  - Protein Kinase C
  - Others

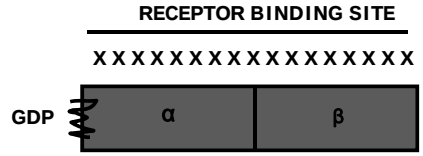
## Protein Kinases

- Has four subunits
- Two Regulatory Subunits
  - Where cAMP binds
- Two Catalytic Subunits
  - Puts Phosphate groups on Ions
  - Is the working part of the enzyme

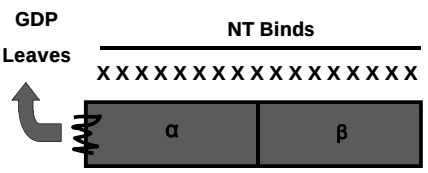


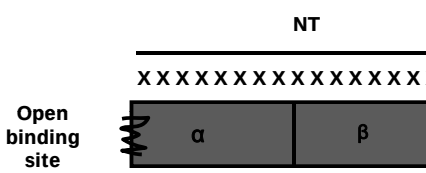
## Gs Proteins Sequence

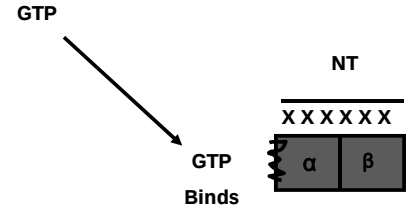
- NT
- Binds to the Receptor
- Causes GDT to leave
- GTP binds – Alpha and Beta Subunits dissociate
- Result – Free Alpha and Free Beta
- Alpha binds to AC
- Causes AC to make cAMP
- cAMP binds to Regulatory Subunit of PK
- Dissociates the PK
- Free Regulatory and Catalytic subunits
- Catalytic subunit phosphorlates (puts a phosphate group of the channel)
- Ions enter the membrane
- Depolarization



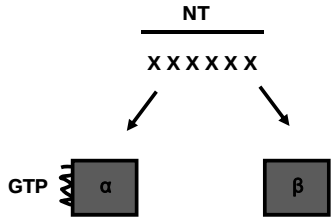

- Stimulation begins



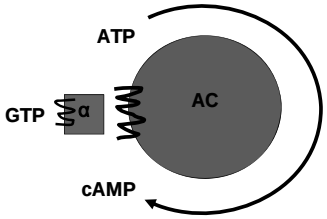



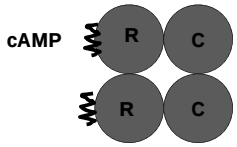

## Dissociation Occurs

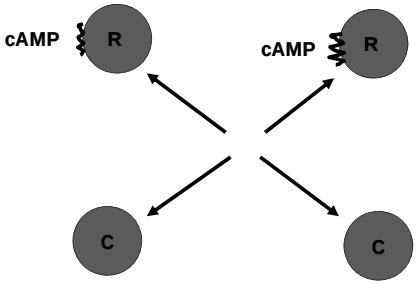


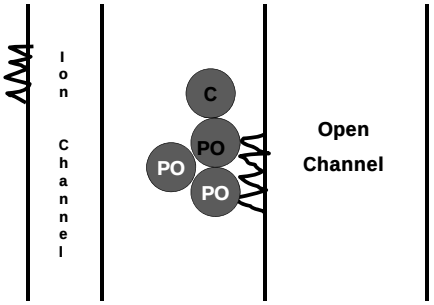
## Adenylyl Cyclase (AC)

- When activated makes cAMP from ATP



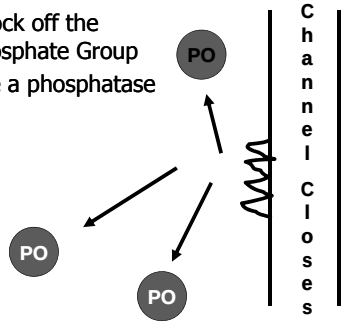



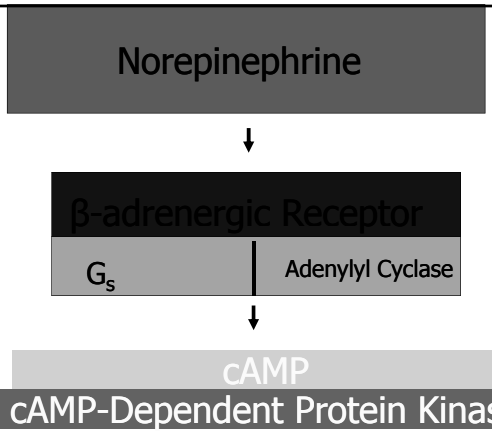




## How to Shut Down the Channel

- Knock off the Phosphate Group
- Use a phosphatase



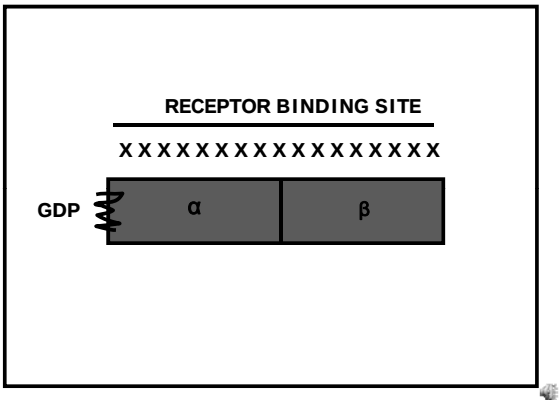
## Gi Proteins

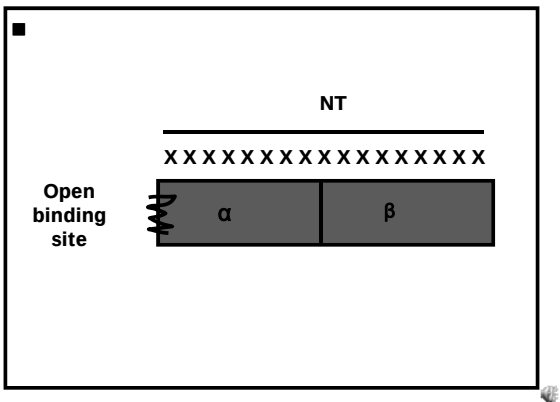
## Gi Proteins

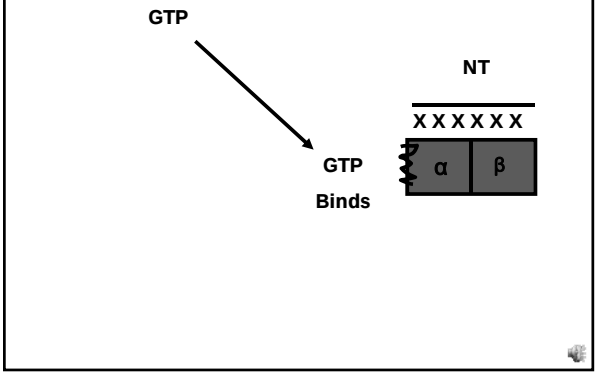
- Are not the same as Gs Proteins
- Causes a decrease in cAMP levels
- Alpha subunits are the different
- Beta subunits are same

## Gi Proteins Sequence

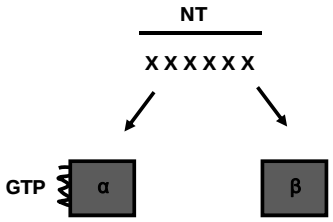
- NT
- Binds to the Receptor
- Causes GDT to leave
- GTP binds – Alpha and Beta Subunits dissociate
- Result – Free Alpha and Free Beta subunits
- Beta subunits begin to bind with Alpha S subunits
- Begin to decrease the activity of Adenylyl Cyclase
- Decreases cAMP production



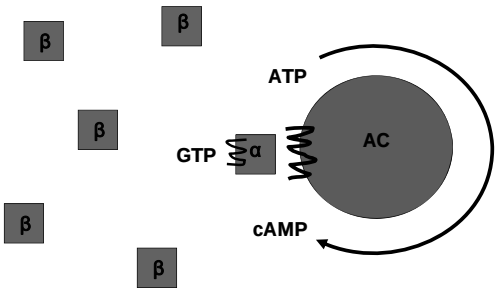



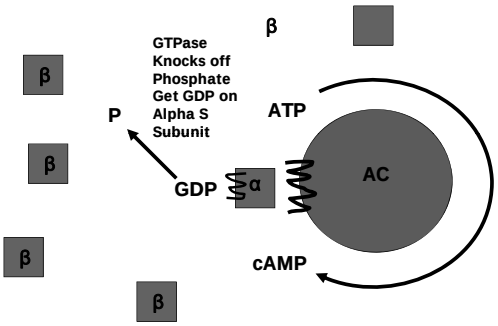
## Dissociation Occurs



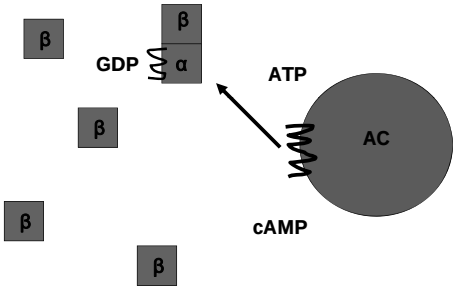

## Adenylyl Cyclase (AC)




## Adenylyl Cyclase (AC)




## Adenylyl Cyclase (AC)

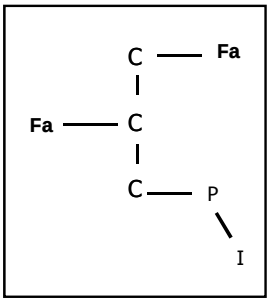



- Decrease of cAMP
- Fewer PK dissociate
- Fewer ion channels open
- Less Depolarization

## Gp Proteins
## Phosphoinositol System

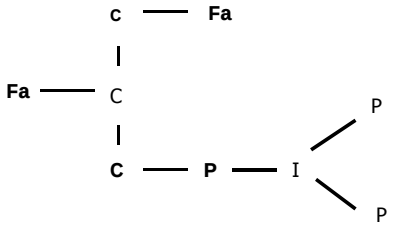
## Phosphoinositol

- Basic Structure



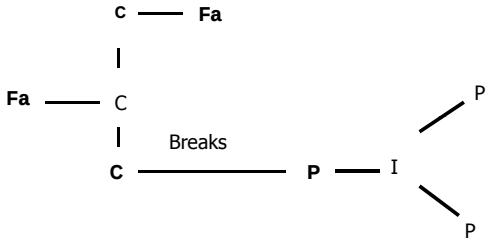

## Can Phosphorlate Two or More Times

- Get Triphosphoinositol



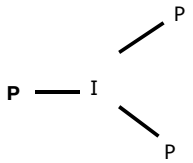

## Gp Proteins Sequence

- NT
- Binds to the Receptor
- Causes GDT to leave
- GTP binds – Alpha P and Beta Subunits dissociate
- Result – Free Alpha P and Free Beta subunits
- Alpha P subunit activates Phospholipase C (Has 9 different forms)
- Phospholipase C splits Triphosphoinositol and breaks it into two groups
- DAG IP-3



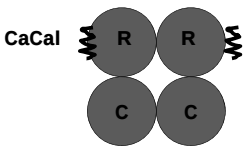

## IP-3 System

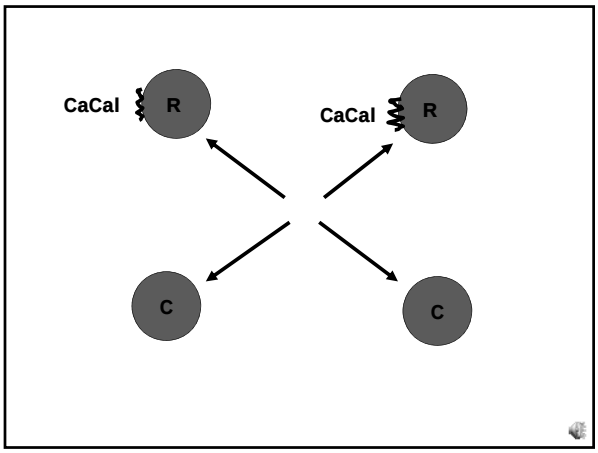
- Is a potent releaser of Ca from smooth ER
- Get a surge of intracellular Ca
- Ca binds with Calmodulin
- CaCal stimulates CaCal protein Kinase
- CaCal PK phosphorlates the ion channel
- Get depolarization

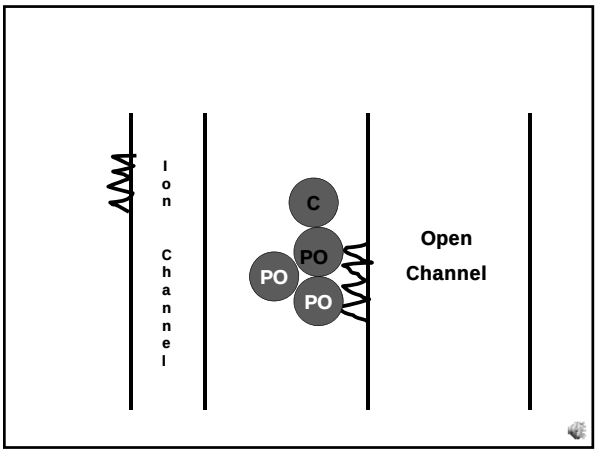



## CaCal Protein Kinase

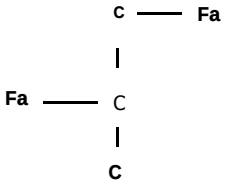
- Similar to cAMP PK
- Has four subunits
- Two Regulatory Subunits
  - Where CaCal binds
- Two Catalytic Subunits
  - Puts Phosphate groups on Ions





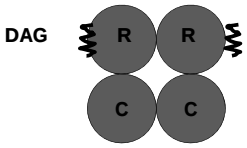

## Diacylglyceral (DAG) System

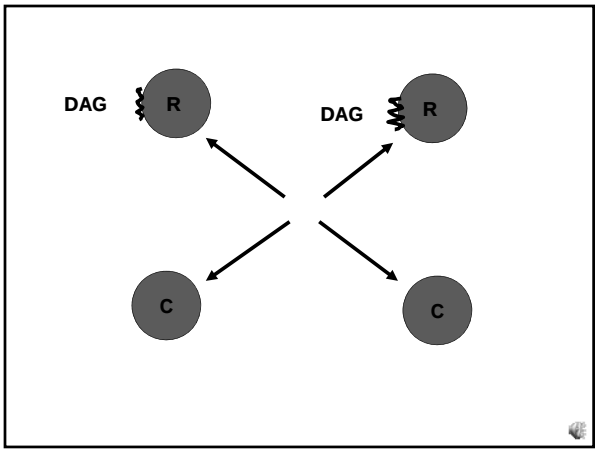


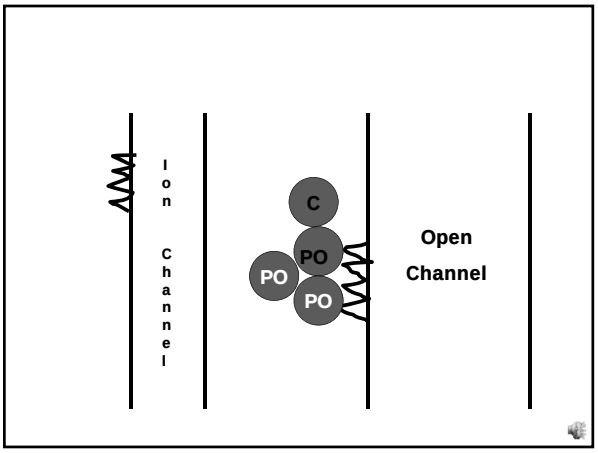

- DAG binds with Protein Kinase C
- Increases the affinity for Ca
- Ca Binds with PK-C
- Causes Phosphorlation
- Channel opens
- Depolarization

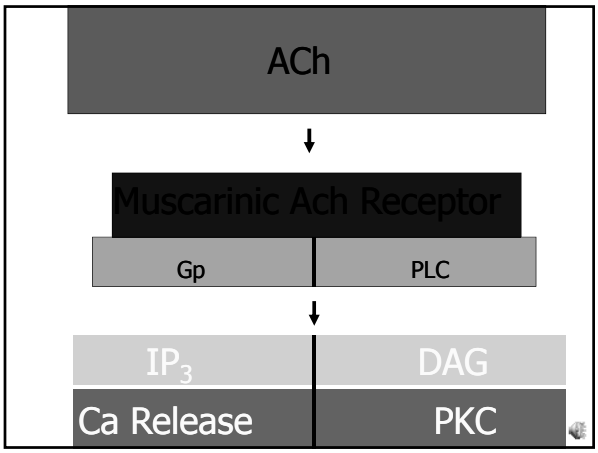
## DAG Protein Kinase

- Similar to other PK
- Has four subunits
- Two Regulatory Subunits
  - Where DAG binds
- Two Catalytic Subunits
  - Puts Phosphate groups on Ion Channel

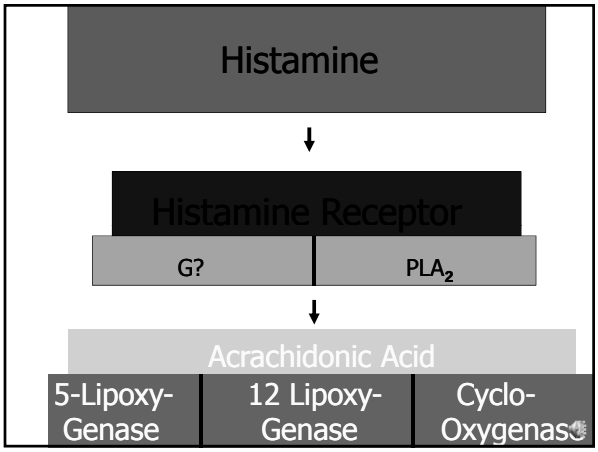





## Arachidonic Acid System




## 3 Sites of Action but Many More

| 5-Lipoxy - Genase | 12 Lipoxy - Genase | Cyclo-OxyGenase |
|---|---|---|
| Several Active Metabolites | Leukotrienes | Prostaglandins and Thromboxanes |
| | | Inhibited by ASA and nonsteroidal antiinflamatory drugs |

## Summary

- Many types
- Hot area of Neurophysiology and Neurochemistry
- Are affected by many psychotropic drugs.