Discussion Session 6
Lectures XII & XIII     Oct 14, 2005

Important stuff

- Review Session? Location TBA…
  - Monday Oct 17 (7-9pm) OR
    Tuesday Oct 18 (7-9pm)
- Problem Set 6
  - DUE WEDNESDAY Oct 19 (this is before Fall Break)
Stuff for Today

- G-protein signaling
  - β-Adrenergic Signaling
  - Metabotropic Glu receptors
- Diseases, toxins and bears oh my!

GPCRs - Metabotropic

- Very important medically
  - 50% of drugs target GPCRs
- Neurotransmitter (ligand) binds to a receptor which activates a 2nd messenger system (via G-proteins)
- Slower, longer lasting response
β-adrenergic Signaling

- Importance: Found in heart and kidney
  - β blockers - lower blood pressure

Metabotropic GluR

- Importance: Involved in slower glutamate post-synaptic responses
Disease & Toxins

- **Diseases**
  - Hyperkalaemic periodic paralysis
  - Lambert-Eaton myasthetic syndrome

- **Toxins**
  - The best thing to happen to neuroscience since sliced brains

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Hyperkalaemic Paralysis

- **Mutation in skeletal muscle voltage-Na channel**
  - (channel becomes leaky)

- **Symptoms**
  - Myotonia (muscle stiffness) - Increased excitability
  - Paralysis - Inactivation of Na channels

- **Precipitated by K rich foods and exercise**

![Diagram of normal and abnormal voltage-gated Na channels](image)
LEMS

- Another autoimmune disease
  - How do you detect an autoimmune disease?
- ABs against presynaptic Voltage-Ca\(^{++}\) channel at NMJ
- What will this do?
  - Decrease amount of Ca\(^{++}\) in presynapse
    - Decrease vesicle release
  - Muscle weakness
- Causes:
  - Cancer induced (60% of the cases)
- Treatment
  - K\(^{+}\) channel blockers; plasma exchange

Toxins (plant, animal etc)

- Hundreds of uses and counting
- Molecular biology uses
  - K/Na conductances in Squid action potential
    - TTX (tetrodotoxin) - blocks Na channels
    - TEA (tetraethylammonium) - blocks K channels
      - Charybdoxin (CTX) very similar
  - Determination of channel structure
    - Mutate toxin or channel to determine structure of channel
  - Visualization of the NMJ
    - \(\alpha\)-bungarotoxin irreversibly binds to nAChR’s
      - Used to monitor development of NMJ
Toxins

- **Medicine**
  - Botulinum toxin (Botox)
    - Inhibits vesicle release
    - Used as treatment for dystonia (syndrome characterized by simultaneous contraction of opposing muscles)
      - Ex. Often develops in highly specialized muscle groups (e.g. violinists hands)
  - Atropine - muscarinic antagonist used to treat asthma
  - Understanding toxin action can lead to designer drugs
    - Keep the parts of the toxin that are helpful, remove the components that have unwanted side-effects

Assignments…

- Problem Set 6 (due next WEDNESDAY)
- Read Chapters 1-8, 23-24
- Look at class website for old midterms and midterm review