Hyperekplexia - Background

- Extremely rare disease which causes stiffening of the muscles in response to startling
  - Less than 200 human cases documented
- Newborns exhibit tonic muscle spasms for first year of life
  - NOT associated with epileptic seizures
  - Tonic muscle spasms can cause SIDS
- Hereditary
- Glycine receptor probably involved
- Famously observed in some goats
Glycine Receptors

- Found only in the brain stem and spinal cord

- Permeable to chloride ions
  - Nernst potential below resting potential

- Mediate fast synaptic inhibition
  - Good candidate for significant control of motor action
Heritability

- **Dominant Form**
  - Responsible for 80% of cases
  - Involves mutations in pore-lining regions (TM2) of the α-subunit

- **Recessive Form**
  - Usually involves mutations in TM1 of the α-subunit
  - Not the pore-lining region

Harvey et al, 2008
Heritability

- Mutations in the β-subunit also implicated
  - Area of active research

- Mutations in GlyT2
  - Glycine synaptic reuptake transporter

Harvey et al, 2008
More About the Dominant Form

- Mutations in TM2 decrease the receptor’s sensitivity to ethanol
- Ethanol is an agonist at the glycine receptor
- Ability of ethanol to enhance receptor function is impaired
- This disease can affect the response of affected patients to certain drugs
Treatment

- Main course of treatment is either clonazepam or diazepam

- Generally ineffective at alleviating symptoms due to affinity for GABA receptors
Questions?