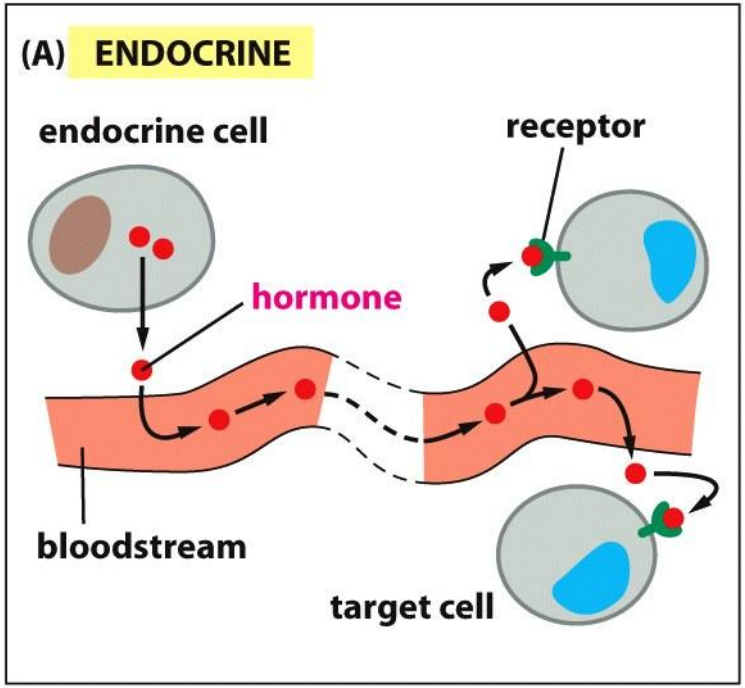
Biochem 03 Cell Communication

November 6, 2009

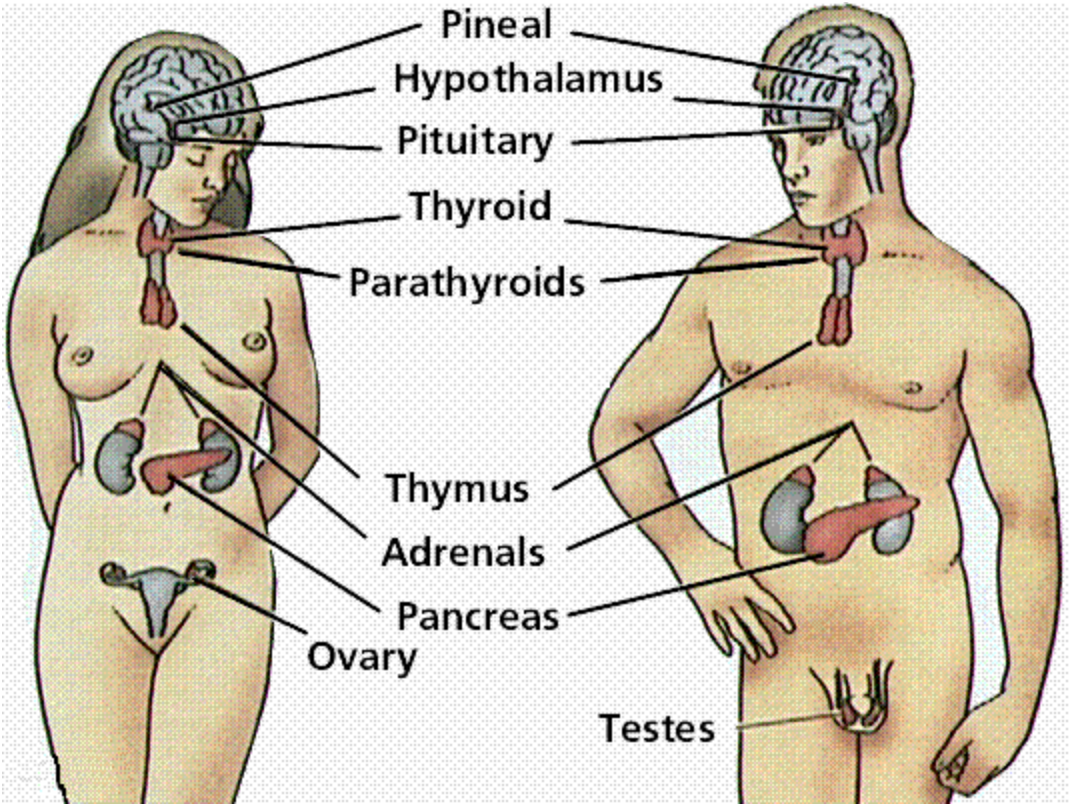
Function: Signal Transduction

- Steroid Hormones
  - Long term acting signals
- **Peptide Hormones**
  - **Various modes of action**
- **Second Messengers**
  - **IP3**
  - **Ca(II)**
  - **Calmodulin**

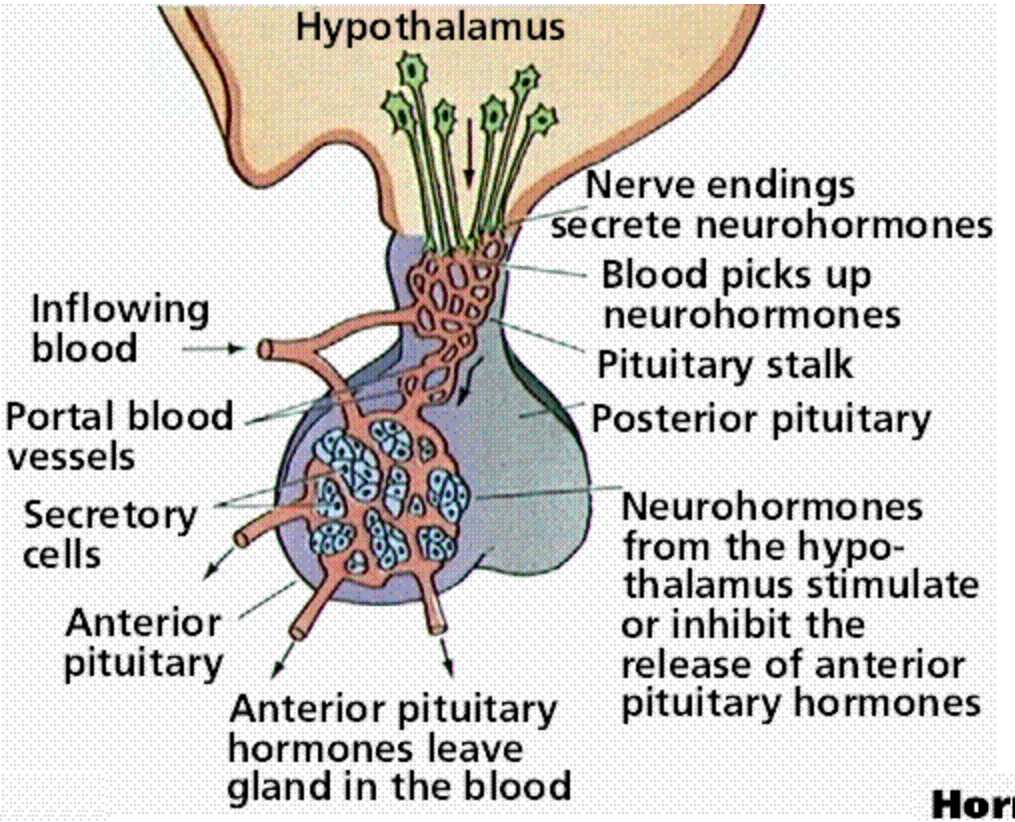


Endocrine System

- **Steroid Hormones**
  - Primary source of these molecules are the ovaries and testes
- **Peptide Hormones**
  - Primary source for these molecules are the rest of the endocrine system: hypothalmus, pineal, pituitary, thyroid, pancreas



Endocrine System Mission Control



Anterior Pituitary

Hormones produced and released:

Thyrotropin
Adrenocorticotropin
Luteinizing hormone
Follicle-stimulating hormone

Growth hormone
Prolactin
Melanocyte-stimulating hormo
Endorphins
Enkephalins

Most of these are PEPTIDE HORMONES

Posterior Pituitary

Hormones released:

Oxytocin
Vasopressin

TABLE 16–1 SOME EXAMPLES OF SIGNAL MOLECULES

SIGNAL MOLECULE	SITE OF ORIGIN	CHEMICAL NATURE	SOME ACTIONS
Hormones			
Adrenaline (epinephrine)	adrenal gland	derivative of the amino acid tyrosine	increases blood pressure, heart rate, and metabolism
Cortisol	adrenal gland	steroid (derivative of cholesterol)	affects metabolism of proteins, carbohydrates, and lipids in most tissues
Estradiol	ovary	steroid (derivative of cholesterol)	induces and maintains secondary female sexual characteristics
Glucagon	α cells of pancreas	peptide	stimulates glucose synthesis, glycogen breakdown, and lipid breakdown, e.g., in liver and fat cells
Insulin	β cells of pancreas	protein	stimulates glucose uptake, protein synthesis, and lipid synthesis, e.g., in liver cells
Testosterone	testis	steroid (derivative of cholesterol)	induces and maintains secondary male sexual characteristics
Thyroid hormone (thyroxine)	thyroid gland	derivative of the amino acid tyrosine	stimulates metabolism of many cell types

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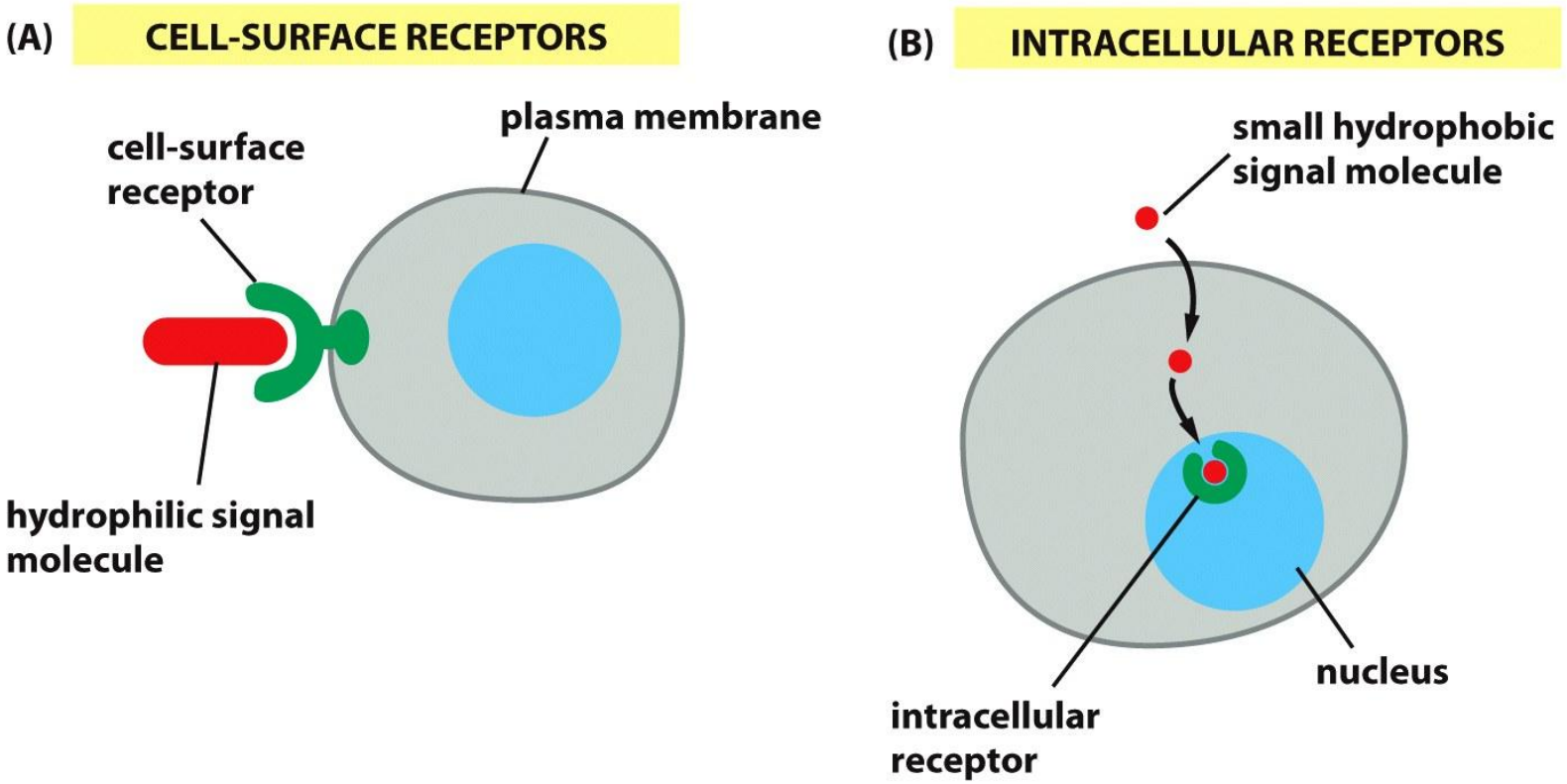
Hormones enter cells through different methods depending on their chemical nature



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Peptide hormones

Steroid hormones

Peptide Hormones---Vasopressin

- Vasopressin is also known as arginine vasopressin (AVP), and antidiuretic hormone (ADH)
- Vasopressin is a peptide hormone that contains just nine amino acids

Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly

- The precursor protein molecule is 164 amino acids and is made in the hypothalamus
- The processes vasopressin is stored in vesicles at the posterior pituitary

While most of the vasopressin in the posterior pituitary will be released into the blood stream; some of it is also released directly into the brain

Peptide Hormones---Vasopressin **Function**

- Primary role of vasopressin is to regulate the body's retention of water; it is released when the body is dehydrated and causes the kidneys to conserve water, thus concentrating the urine and reducing urine volume
- In high concentrations, it also raises blood pressure by inducing moderate vasoconstriction
- The main stimulus for secretion of vasopressin is increased osmolality (?) of blood plasma. Reduced volume of extracellular fluid also has this effect, but is a less sensitive mechanism

- Osmolality =
- The AVP that is measured in peripheral blood is almost all derived from secretion from the posterior pituitary gland

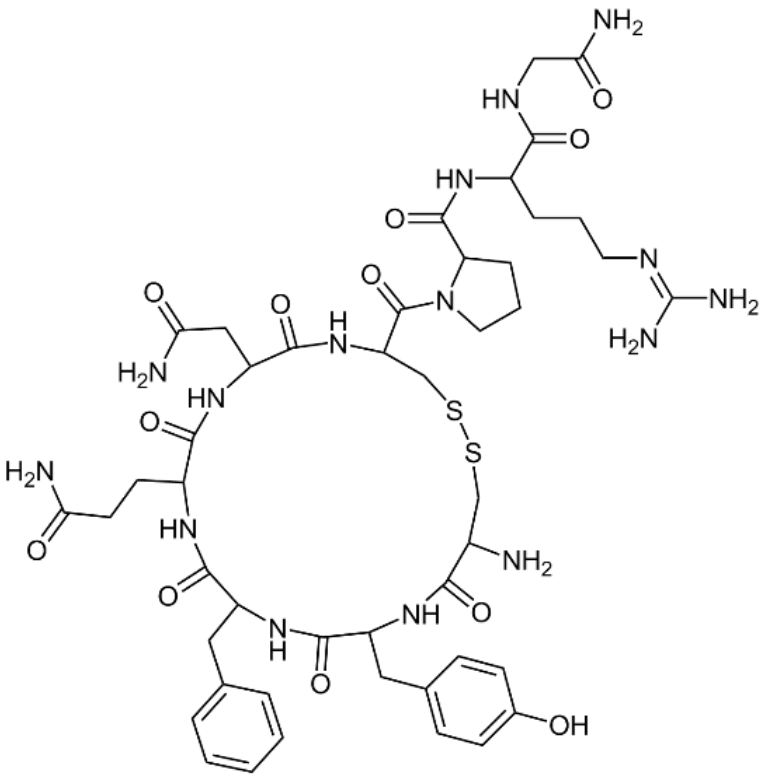
Peptide Hormones---Vasopressin **Function**

- In addition, vasopressin has a variety of neurological effects on the brain, having been found, for example, to influence pair-bonding in small mammals
  - Evidence for this comes from experimental studies in several species, which indicate that the precise distribution of vasopressin and vasopressin receptors in the brain is associated with species-typical patterns of social behavior
  - In particular, there are consistent differences between monogamous species and promiscuous species in the distribution of vaso. receptors, and sometimes in the distribution of vasopressin-containing axons, even when closely-related species are compared

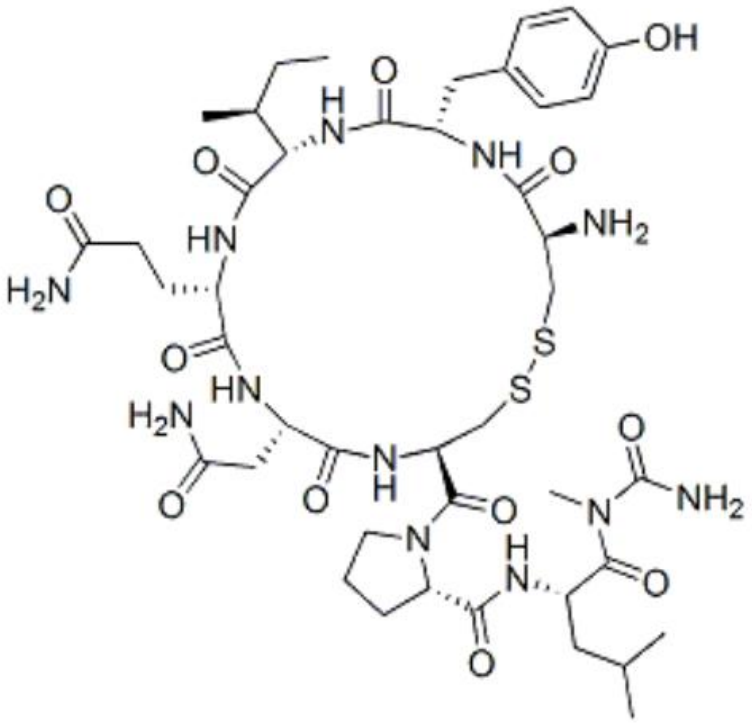
Vasopressin is very similar to another class of hormones, oxytocin

Vertebrate Vasopressin Family		
Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH2	Argipressin (AVP, ADH)	Most mammals
Cys-Tyr-Phe-Gln-Asn-Cys-Pro-Lys-Gly-NH2	Lypressin (LVP)	Pigs, hippos, warthogs, some marsupials
Cys-Phe-Phe-Gln-Asn-Cys-Pro-Arg-Gly-NH2	Phenypressin	Some marsupials
Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Arg-Gly-NH2	Vasotocin†	Non-mammals
Vertebrate Oxytocin Family		
Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Leu-Gly-NH2	Oxytocin (OXT)	Most mammals, ratfish
Cys-Tyr-Ile-Gln-Asn-Cys-Pro-Ile-Gly-NH2	Mesotocin	Most marsupials, all birds, reptiles, amphibians, lungfishes, coelacanths
Cys-Tyr-Ile-Gln-Ser-Cys-Pro-Ile-Gly-NH2	Seritocin	Frogs
Cys-Tyr-Ile-Ser-Asn-Cys-Pro-Ile-Gly-NH2	Isotocin	Bony fishes

Both peptides cyclize through the two cysteine residues



Vasopressin: cys-tyr-phe-gln-asn-cys-pro-arg-gly

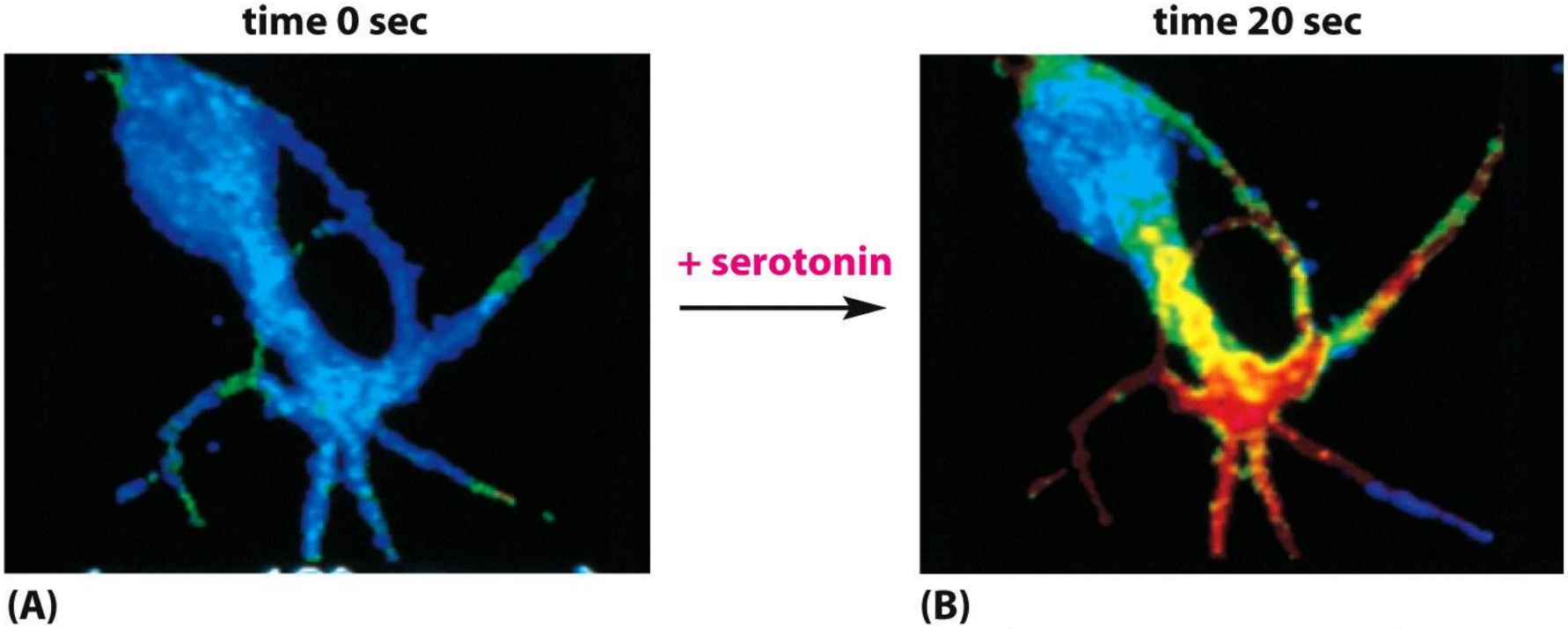


Oxytocin: cys-tyr-ile-gln-asn-cys-pro-arg-gly

Oxytocin's Function

- **Primary:**
  - powerful uterine contractions at birth
  - Lactose release from the mammary glands (let down reflex)
- **Secondary (neurological)**
  - Oxytocin effects in humans were recently demonstrated by a behavioural study showing selectively increased trust after hormone administration (Kosfeld, M., et al. (2005). Nature, 435: 673-676)
  - neural mechanism for the effects of oxytocin in social cognition in humans and provides a potential therapeutic approach to social anxiety currently being tested in social phobia and autism (oxytocin nasal spray)

Some signaling molecules are derived from amino acids



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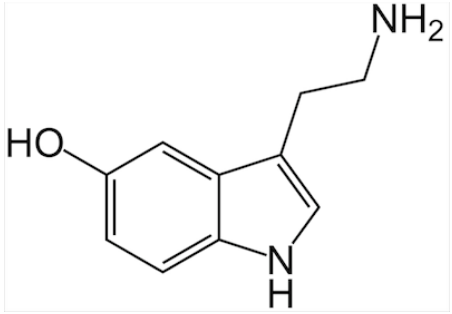


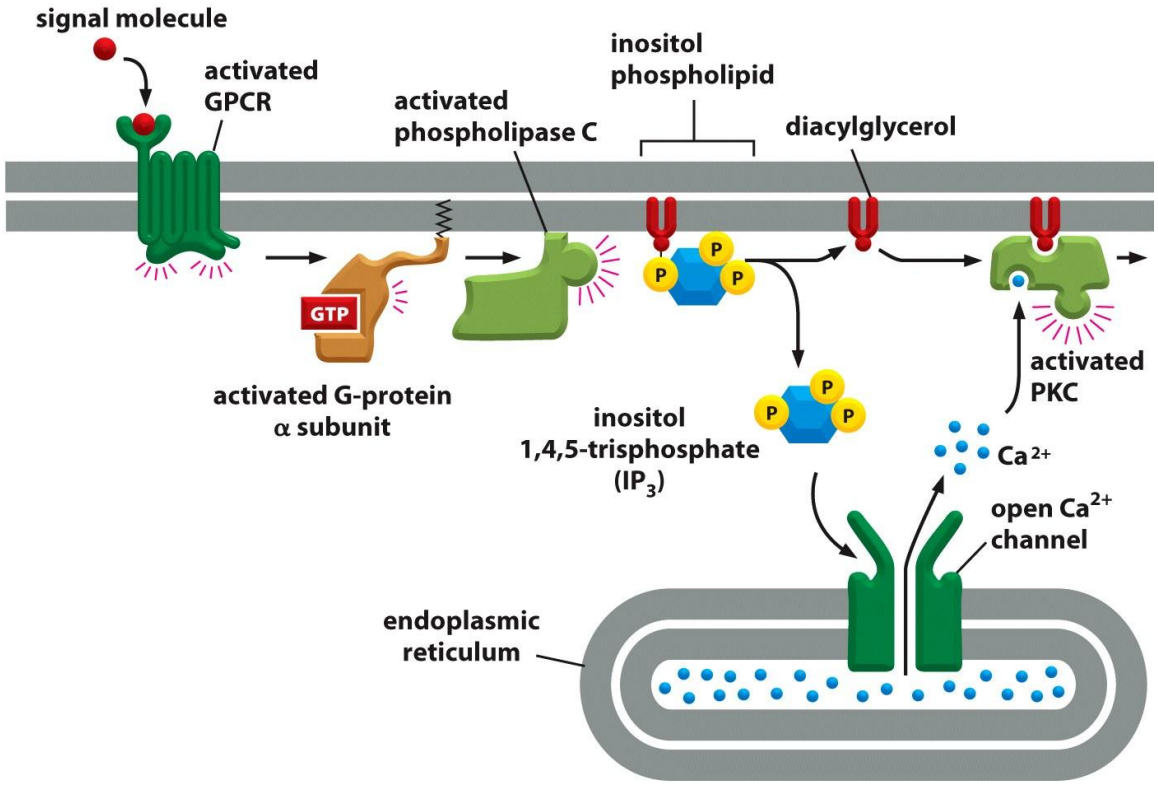
Serotonin is made from Trytophan

Hierarchy of Signaling

- Hormones and other signaling molecules are termed "first messengers"
- When the hormone, signal does not itself enter the cell, how is its signal manifested within the cell?
- Answer: second messengers ---intracellular molecules or ions that translate the primary signal into the local environment

Second Messenger: IP_3

- Some cells respond to a signal by changing the structure of a molecule in the membrane
  - here cleavage of phospholipid into DAG and a phosphoryllated sugar, IP3
- Cell response is that calcium is released from intracellular storage vessels



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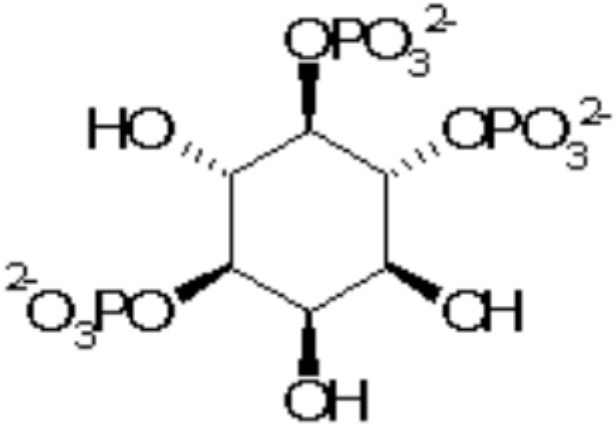
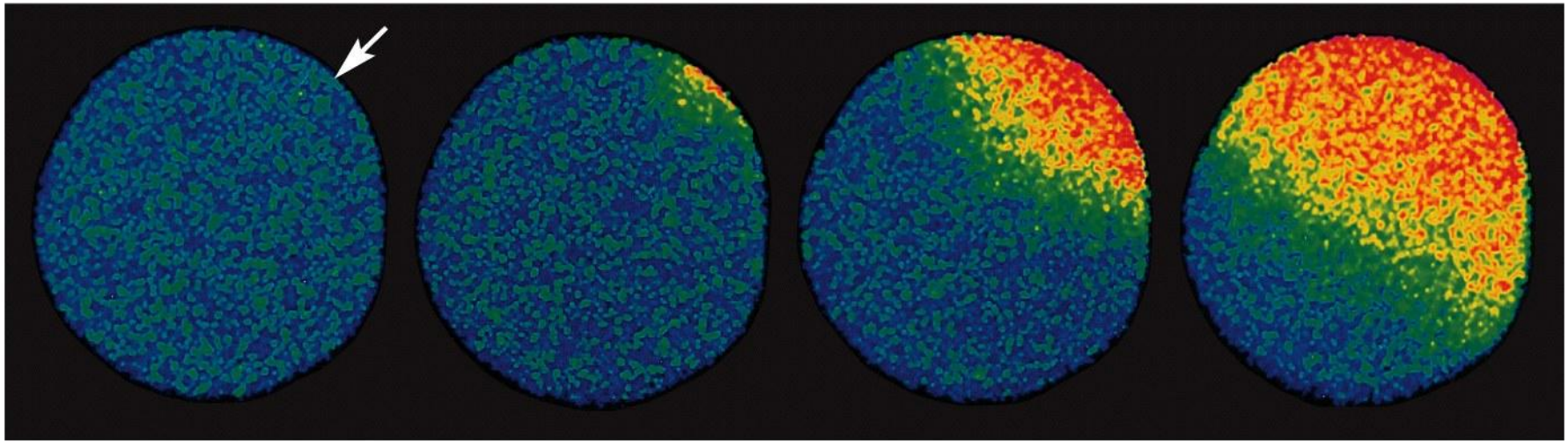
Second Messenger: IP_3

- IP3 chemical structure
- Inositol triphosphate
- How is this sugar different from glucose or the other sugars that we examined?



- Is this a polar molecule?

Second Messenger: Ca(II) and CaM



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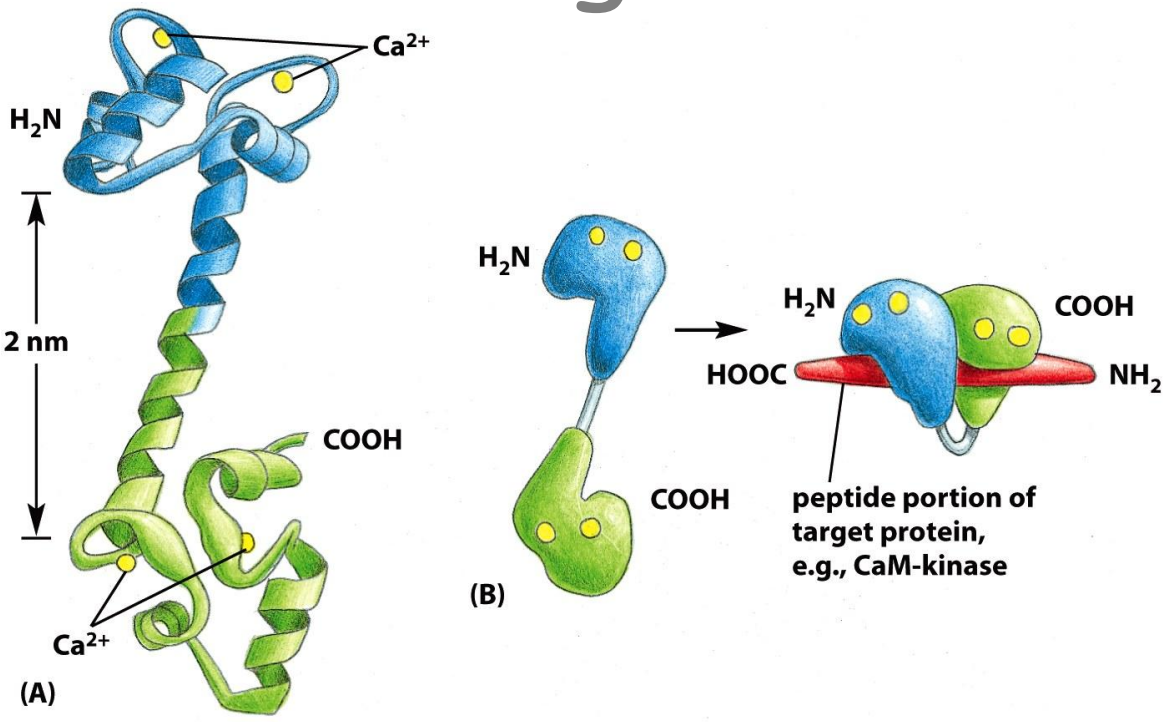
Ca(II) wave within cell

Second Messenger: Ca(II) and CaM

Problems with Ca(II) within living cells

1. Normally, intracellular Ca(II) (soluble) is $<10^{-6}$ M
2. Extracellular fluids are 10^{-3} M
3. Gradient is >1000x
4. Why?

Second Messenger: Ca(II) and CaM



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- When the cell is given a signal in the form of a shot of Ca(II), it responds by using the protein calmodulin (CaM) to bind to the Ca(II)
- Activated CaM in turn activates other proteins (>36)
- One of the targets of anthrax toxins