Goals and Challenges of Communication

- Reaching (only) the correct recipient(s)
- Imparting correct information
- Timeliness
- Causing the desired effect
- Effective...

Communication and Signal Transduction

How Do Cells Communicate?

- Unit 2 is about cell-cell communication, one of the most heavily researched areas of physiology today
Stuff that Was Confusing

How is it Possible That...

- Chemicals traveling in the bloodstream act only on specific targets?
- One chemical can have different effects on different tissues?
- Cells can change their sensitivity to the chemical through time?

Receptors and Signal Transduction

Hold on to your adenoids...
What Determines the Meaning of a Message?

The Meaning of a Message is determined by:

- The ligand (the thing that binds)
- The receptor (what the thing binds to)

Agonists and antagonists are clinical, synthesized ligands.
Signal Transduction

- Transduction = to send information in a different form

Signal Transduction

- Signal Transduction in a cell refers to the transmission of a signal from 1 side of the cell membrane to the other
- First messenger = Ligand
  - The action of the ligand depends upon it's ability to
There Are Two Possibilities:

- The ligand is lipophilic (CAN cross the membrane)
- The ligand is lipophobic (CANNOT cross the membrane)
What Lipophobic Ligands Bind To

Second Messengers
- Second messengers are intracellular molecules that facilitate transduction of a lipophobic message to the interior of a cell
- These messengers may
  - open or close membrane channels
  - modulate metabolic enzymes
  - activate or deactivate transport proteins

Signal Transduction Pathways Often Have
- Cascade reactions
- Signal amplification
Transduction Mechanisms

- Various types:
  - Tyrosine kinase
    - is a receptor (the ligand binds to it)
    - is a kinase (a phosphorylating enzyme)

Phosphorylation

ACTIVATE MODULATE EXCITE
STIMULATE DEACTIVATE PRODUCE
EXCRETE STOP SECRETE
MOVE INHIBIT TRANSPORT
REGULATE UPTAKE CATALYZE

Transduction Mechanisms

- G protein-coupled receptors (GPCRs)
  - Can link receptors to ion channels
  - Can link receptors to amplifier enzymes:

<table>
<thead>
<tr>
<th>Table 6-1</th>
<th>Amplifier Enzymes</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPLIFIER ENZYME</td>
<td>CELLULAR LOCATION</td>
</tr>
<tr>
<td>Adenylyl cyclase</td>
<td>Membrane</td>
</tr>
<tr>
<td>Guanylyl cyclase</td>
<td>Membrane</td>
</tr>
<tr>
<td>Phospholipase C</td>
<td>Membrane</td>
</tr>
</tbody>
</table>

*IP₃ = inositol triphosphate; DAG = diacylglycerol
What IS cyclic AMP?

ATP \rightarrow \text{adenylyl cyclase} \rightarrow \text{cAMP}

Second Messengers

<table>
<thead>
<tr>
<th>SECOND MESSENGER</th>
<th>MADE FROM</th>
<th>AMPLIFIER ENZYME</th>
<th>LINKED TO</th>
<th>ACTION</th>
<th>EFFECTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>cAMP</td>
<td>ATP</td>
<td>Adenylyl cyclase (membrane)</td>
<td>GPCR*</td>
<td>Activates protein kinase A, especially PKA.</td>
<td>Binds to ion channels. Alters channel opening.</td>
</tr>
<tr>
<td>cGMP</td>
<td>GTP</td>
<td>Guanylyl cyclase (membrane)</td>
<td>Receptor-enzyme</td>
<td>Activates protein kinase G (PKG).</td>
<td>Binds to ion channels. Alters channel opening.</td>
</tr>
<tr>
<td>IP_3</td>
<td>Membrane phospholipids</td>
<td>Phospholipase C (membrane)</td>
<td>GPCR</td>
<td>Releases Ca^{2+} from intracellular stores.</td>
<td>Sees Ca^{2+} effects below.</td>
</tr>
<tr>
<td>DAG</td>
<td>Membrane phospholipids</td>
<td>Phospholipase C (membrane)</td>
<td>GPCR</td>
<td>Activates protein kinase C.</td>
<td>Phosphorylates proteins.</td>
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<td>Ca^{2+}</td>
<td>Membrane phospholipids</td>
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*GPCR = G protein-coupled receptor. IP_3 = inositol triphosphate. DAG = diacylglycerol.
Endocrinology

Long-distance signalling may be electrical signals passing along neurons or chemical signals that travel through the circulatory system.

**Endocrine System**

(d) Hormones are secreted by endocrine glands or cells into the blood. Only target cells with receptors for the hormone respond to the signal.
What is a Hormone?

- Hormones act on distant target(s) and are effective at very low concentrations
- Hormones have half-lives
- Hormones must be transported via the blood to distant target(s)
- Hormones control:
  - Growth and development
  - Metabolism
  - Homeostasis
  - Reproduction

Hormones act on target cells by controlling:

- Rate of enzymatic reactions
- Membrane transport
- Other hormones (trophic hormones)

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<table>
<thead>
<tr>
<th>Nervous System</th>
<th>Endocrine System</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST</td>
<td>SLOW</td>
</tr>
<tr>
<td>Electrochemical</td>
<td>Chemical signals</td>
</tr>
<tr>
<td>signals</td>
<td></td>
</tr>
<tr>
<td>Short duration</td>
<td>Long duration</td>
</tr>
<tr>
<td>Neurons</td>
<td>Secretory cells</td>
</tr>
</tbody>
</table>

Hormone Classification

- Anatomical Classification:
  - "Classic" (secreted by endocrine cells)
- Neurosecretory (secreted by neurons)

- Chemical Classification:
  - Peptide hormones
  - Steroid hormones
  - Amine hormones
Chemical Classes of Hormones
Yippee! There are Only THREE CLASSES:

- Amine Hormones: Catecholamines
- Peptide hormones
- Steroid hormones
- Thyroid hormones

For Each Class You Need to Know:

- How is it made?
- How is it secreted?
- How is it transported through the body?
- What is its mechanism of action?
- How long does its message last (half-life)?

KEEP IN MIND

The lipid solubility of the hormone will determine a lot about its behavior.
Peptide Hormones

- Peptide Hormone Synthesis
  - Synthesized in rough ER, processed in ER and Golgi
  - Preprohormone --> prohormone --> hormone
  - Hormone is then packaged in secretory vesicles by the Golgi and stored
  - Vesicle contents released by Ca++ dependent exocytosis

Peptide Transport and Half-Life

- Peptides are water-soluble, and dissolve in extracellular fluid for transport

  - Half-lives are short (several minutes)

Cellular Mechanisms of Action

- Peptides are lipophobic, so they have membrane receptors.
- Signal transduction sets off cell response (usu. cAMP)
Steroid Hormones

- Derived from cholesterol
- Made only in gonads, placenta, and adrenal cortex
- How can a cell store them?

Steroid Hormone Transport and Half-Life

- Steroids are transported by protein carriers
- Long half-life
Cellular Mechanisms of Action of Steroid Hormones

- Intracellular receptors in cytoplasm or nucleus of target cell
- Many are transcription factors / interact with
- High lag time

Amine Hormones

- Amine hormones are derived from single
- Melatonin (tryptophan)
- Catecholamines and thyroid hormones (tyrosine)
Catecholamines

- Catecholamines are synthesized in neural tissue.
- Synthesis, release, and cellular mechanism of catecholamines are similar to peptide hormones.

Thyroid hormones

- Synthesized like peptide hormones, but behave like steroid hormones once released.
- Contain iodine.
- Like peptide hormones, thyroid hormones are made in advance and stored in an inactive form.

Transport and Half-Life of catecholamines:

- They are lipophobic and dissolve in the plasma. In the blood, they have a very short half-life (seconds).

Cellular Mechanism of Action:

- They bind to membrane receptors and modify existing proteins to exert their actions.
Thyroid hormones

- Require [ ] to be transported in the blood.
- Thyroid-receptor complex activates transcription.

Control of Hormone Release

We classify hormones by endocrine reflex pathways

- Classic hormones
  - Endocrine cell acts as a receptor, integrating center and [ ]
  - Ex: Parathyroid hormone
Classic hormones with multiple controls (stimuli)

- Ex: secretion is affected by:
  - Blood glucose levels
  - Nervous system activities
  - Hormones secreted by cells in small intestine

Neurohormones

- Are released when a nerve cell that synthesizes them receives a signal from the nervous system
How Hormones Interact

Hormones act together on a target

- "The whole is greater than the sum of the parts"
- Ex: epinephrine and glucagon on elevation of blood glucose

Permissiveness

- One hormone cannot act without the presence of another hormone
- Ex: Thyroid hormone must be present, along with GRH, gonadotropins and steroid hormones for normal development of the system
Antagonism

- One hormone counteracts the effects of another

- Ex: growth hormone or glucagon both increase blood glucose and are antagonistic to insulin.