Biochemical Classes of Drug Targets of Current Therapies

N = 483

- Receptors, 45%
- Enzymes, 28%
- Hormones & factors, 11%
- DNA, 2%
- Ion channels, 5%
- Nuclear receptors, 2%
- Unknown, 7%
RECEPTOR = protein that carries out recognition and amplification

- Typically receptors bind to a signaling molecule and undergo a conformational change that "switches on" or "off" a protein activity or function.

Endogenous signaling molecule is called the **AUTO**
The gain (or loss) of protein activity leads to amplification of the signal "sent" by the autocoicid.

See examples:
These will be posted on course website see syllabus for URL.
Examples of receptors

**Nerve Junctions**

Binding of single neurotransmitter activates cyclase enzyme... millions of cAMP molecules are produced.

neurotransmitter

reuptake receptor: a single protein removes 1000's of neurotransmitters from the junction
Nuclear receptors

\[ a + b \rightarrow c \]

"off"  "on"

DNA

Gene expression

Bind of a single ligand to the receptor "switches on" DNA-binding activity. Leads to transcription of multiple mRNA molecules that are, in turn, converted to proteins.
Ligand-Gated Channels & pumps

Binding of a single autacoid opens the channel... thousands of K⁺ ions flow from the cell.
Drugs can do two things...

AGONIST - mimics the action of the autacoid

ANTAGONIST - blocks the action of the autacoid
Tools for measuring drug action.

\[
C + \text{receptor} \rightleftharpoons C \cdot \text{receptor}
\]

\[
K_d = \frac{[C][\text{receptor}]}{[C \cdot \text{receptor}]}
\]

\[
K_d = \text{conc. required for 50% activity}
\]

- Log [C]

Low conc

High conc
Why use $-\log [c]$?

% Biol act.

[drug]

From regular plot, it is not so easy to "see" $K_d$.
1. Agonist - produces same maximal response as natural substance, not necessarily with same Kd, of course.

- Log [DRUG]
2. Antagonist (competitive) produces no response on its own, but is capable of blocking the action of autocoid at the receptor. Thus, increasing conc of autocoid are required to gain 100% activ.
3. Non-competitive antagonist - Limits the maximal response elicited by the autacoid. Regardless of autacoid conc., maximal 100% response cannot be obtained.

\[ \text{Log} \left[ \text{Autacoid} \right] \]
4. Partial agonist - Elicits a maximal response that is LESS than the autacoid. This type of agent can also act as a partial antagonist under some conditions - preventing full response from autacoid.
Possible Results of Drug-Receptor Interaction...

1. **Agonist** - Produces same maximal response as natural substance. Not necessarily with the same $K_d$, however.

2. **Antagonist** (competitive) - Produces no response of its own, but is capable of blocking the action of the natural signal molecule (autocoid) at the receptor. Increasing concentrations of the autocoid are required to elicit maximal response.

3. **Non-Competitive Antagonist** - Limits the maximal response elicited by the autocoid. Regardless of autocoid concentration, maximal response cannot be obtained.

4. **Partial Agonist** - Maximal response is less than that of the autocoid. Thus, this type of drug can elicit a response at the receptor, but can also antagonize that action of the autocoid at high autocoid concentrations.