Chapter 16

Web Text Box 1

Ionotropic and metabotropic receptors for the same transmitter

In the book we meet a number of transmitter molecules that bind to receptors on target cells. For example we have described how acetylcholine binds to and opens the nicotinic acetylcholine receptor, an ion channel permeable to sodium potassium and sometimes calcium, while ADP binds to and activates a metabotropic receptor that acts through the trimeric G protein G_q to activate phospholipase Cβ and hence generate a cytosolic calcium signal.

In fact many transmitters act at more than one receptor and more than one receptor type. Acetylcholine has another evolutionarily unrelated receptor called the muscarinic acetylcholine receptor. Like the nicotinic acetylcholine receptor this is named for a toxin that binds to it, in this case muscarine from the fly agaric mushroom *Amanita muscaria*. Many muscarinic acetylcholine receptors activate G_q and hence trigger a calcium signal.

There is no ionotropic receptor for ADP, but there is a whole family of ionotropic receptors for ATP, called the P2X receptors (P stands for purine). These have a wide range of functions and even mediate synaptic transmission in some locations in the body (for a review see Burnstock. 2006. Trends in Pharmacological Sciences, 27:166).

The table below shows some other cases where multiple receptor types exist for the same transmitter. Black text indicates receptors mentioned in the book while red text indicates another receptor for the same transmitter.

It is because there are often more than one receptor for a transmitter that the names of receptors are often cumbersome. For example we need to specify “nicotinic acetylcholine receptor” to distinguish this protein from the muscarinic acetylcholine receptor.

Black text indicates receptors mentioned in the book while red text indicates another receptor for the same transmitter.	
Ionotropic receptor	**Metabotropic receptor**
Ionotropic GABA receptor (also called $GABA_A$ receptor) An ion channel that opens when GABA binds to its extracellular aspect. Selective for chloride. Described on page 273 of the book.	***Metabotropic GABA receptor*** (also called $GABA_B$ receptor) A metabotropic receptor that acts through two G protein isoforms that we do not describe in the book, G_i and G_o. Classically G_i inhibits adenylate cyclase and therefore reduces the concentration of cytosolic cAMP, but it is now realized that the G_i/G_o family of G proteins has a wide range of targets including ion channels.
Ionotropic glutamate receptor An ion channel that opens when glutamate binds to its extracellular aspect. Permeable to sodium and potassium, some isoforms also pass calcium. Described on page 269 of the book.	***Metabotropic glutamate receptor*** A family of G protein coupled receptors. When glutamate binds to their extracellular aspect they become guanine nucleotide exchange factors for trimeric G proteins. Some isoforms activate G_q, and therefore cause a calcium signal. Others act through G_i and G_o (see above).
Nicotinic acetylcholine receptor An ion channel that opens when glutamate binds to its extracellular aspect. Permeable to sodium and potassium, some isoforms also pass calcium. Described on page 274 of the book.	***Muscarinic Acetylcholine Receptor*** A family of G protein coupled receptors. When glutamate binds to their extracellular aspect they become guanine nucleotide exchange factors for trimeric G proteins. Some isoforms activate G_q, and therefore cause a calcium signal. Others act through G_i and G_o (see above).
P2X receptors A family of ionotropic receptors that open when ATP binds to their extracellular aspect. Permeable to sodium, potassium and calcium.	***P2Y receptors*** A family of G protein coupled receptors that are activated when nucleotides bind to their extracellular aspect. Some are activated by extracellular UTP, some by ATP and some by ADP (these last are the ADP receptors we discuss on page 253 of the book). Upon activation they become guanine nucleotide exchange factors for trimeric G proteins. One group activate G_q, and therefore cause a calcium signal. The others act through G_i (see above) and therefore reduce the concentration of cytosolic cAMP.