14.2: Receptors and Ligands

A protein that happens to bind something is not necessarily a receptor. A receptor is defined as a protein that binds to an extracellular ligand, and then undergoes a conformational or biochemical shift in such a way that it initiates a chain of intracellular events by which the cell reacts to the extracellular signal. What are these ligands and their receptors?

Intercellular signals span a very wide range of molecule types. Some are simple gases, like NO, while others are amino acids or derivatives, including glutamate, dopamine, or epinephrine. Lipids such as steroids (e.g. estrogen, cortisol) or eicosanoids (e.g. prostaglandins, leukotrienes) can be intercellular messengers. Finally many signals are peptides or even complex proteins (recall our juxtacrine signaling example). Although most are recognized by cell surface receptors, this is not always the case since, for example, steroids are lipid-soluble and can diffuse through the plasma membrane.

Receptors are a far less varied group of molecules, since they are all proteins, though it must be said that they represent many different protein structures and functions. In general, receptors are very specific for their ligands, but the specificity is not mutual: ligands can be rather promiscuous and bind with multiple receptors. This is part of the coordination aspect of signaling, though as a single ligand can initiate different effects in different cells depending on what receptor is expressed. The remainder of this chapter will delve into some of the intracellular signaling cascades that are characteristic of particular receptor types.

Because receptors, even at high density, represent only a minute fraction of the surface area of the cell, and therefore an even tinier fraction of the volume of the cell, the activation of a receptor must be amplified in order for it to initiate cellular activities (e.g. locomotion, growth, cell cycle progression). Thus one of the first things a receptor does upon activation is to initiate a signaling cascade. This aptly named sequence of events begins with the receptor activating an enzyme. The enzyme may be the cytoplasmic domain of the receptor itself, or it may be an independent protein but closely linked to the receptor. The enzyme does what enzymes do: it rapidly converts substrate molecules into product molecules. In this case, sometimes the product is an activator for another enzyme, and sometimes, the substrate is an...
inactive enzyme and the product is an activated enzyme. Either way, because of the high activity rates, the single activation of the receptor has increased first to tens or hundreds of enzyme activations, and each of those activates hundreds, and so on, so that the effect of the receptor can be rapidly distributed throughout the cell.