Signal transduction - exciting research with huge potential for the future

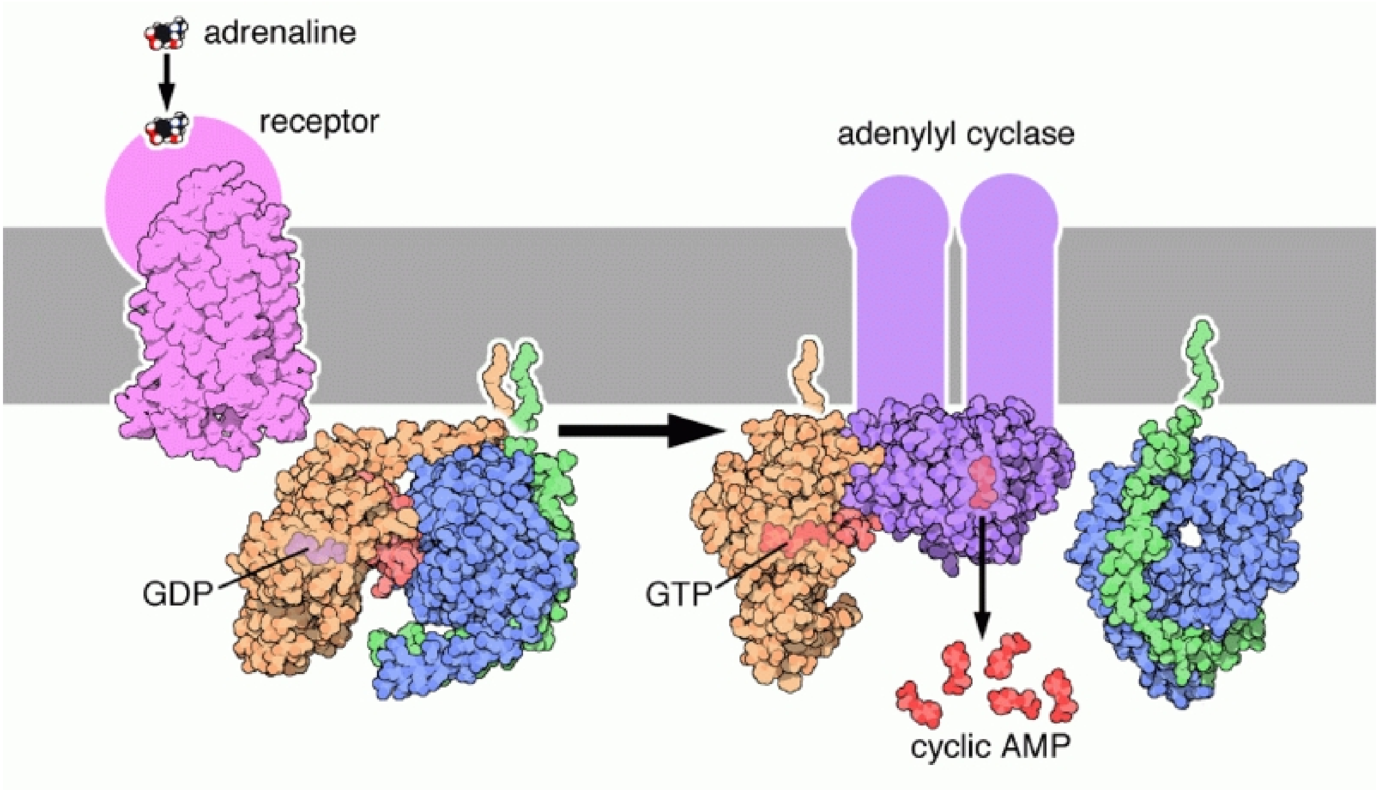
Signal transduction is one of the most innovative fields of research in the life sciences. A book entitled "Molecular Biology of the Cell" is clear evidence of this. When the first edition of the mighty tome was published in the 1980s, Bruce Alberts and his co-authors only devoted a few paragraphs to signal processing and cellular communication. A lot was still unknown and unclear at the time. The current 5th edition devotes a complete chapter to the "Mechanisms of Cellular Communication". Although the scientists are far from being able to understand and decipher everything, the signal researchers nevertheless have a good deal of knowledge about the transduction of signals and the different signalling pathways.

The term "signal transduction" was first used in a scientific paper in 1972. The terms signal transduction or signal transmission are used to describe the processes used by cells to communicate with each other, react to external stimuli, convert them and transmit them into the interior of cells. Multicellular organisms need to communicate with each other in order to exist. Cell-cell communication involves a lot more than just sending a chemical signal from one cell to another. The intracellular mechanisms involved are very complex. It took 2.5 billion years for communication pathways to develop to a degree that enabled unicellular organisms to become multicellular organisms. Signal transduction processes are vital to ensure that unicellular organisms can react to changing environmental conditions. In higher organisms, the transduction of signals is used for the processing of internal and external stimuli.

Defective signalling pathways cause many diseases

The activation of genes, metabolic changes, cell growth, division and death are just a limited number of important examples of processes that are controlled through signalling pathways. The transduction of signals in and between nerve cells is well known. The immune defence is no more than a signal transduction process. Nowadays, it is known that many diseases are the result of defective or missing signalling pathways. For cancer, this was believed to be the case very early on. In the meantime, there has been substantial evidence to show that diabetes, kidney, autoimmune and heart diseases are the result of defective signal transduction.

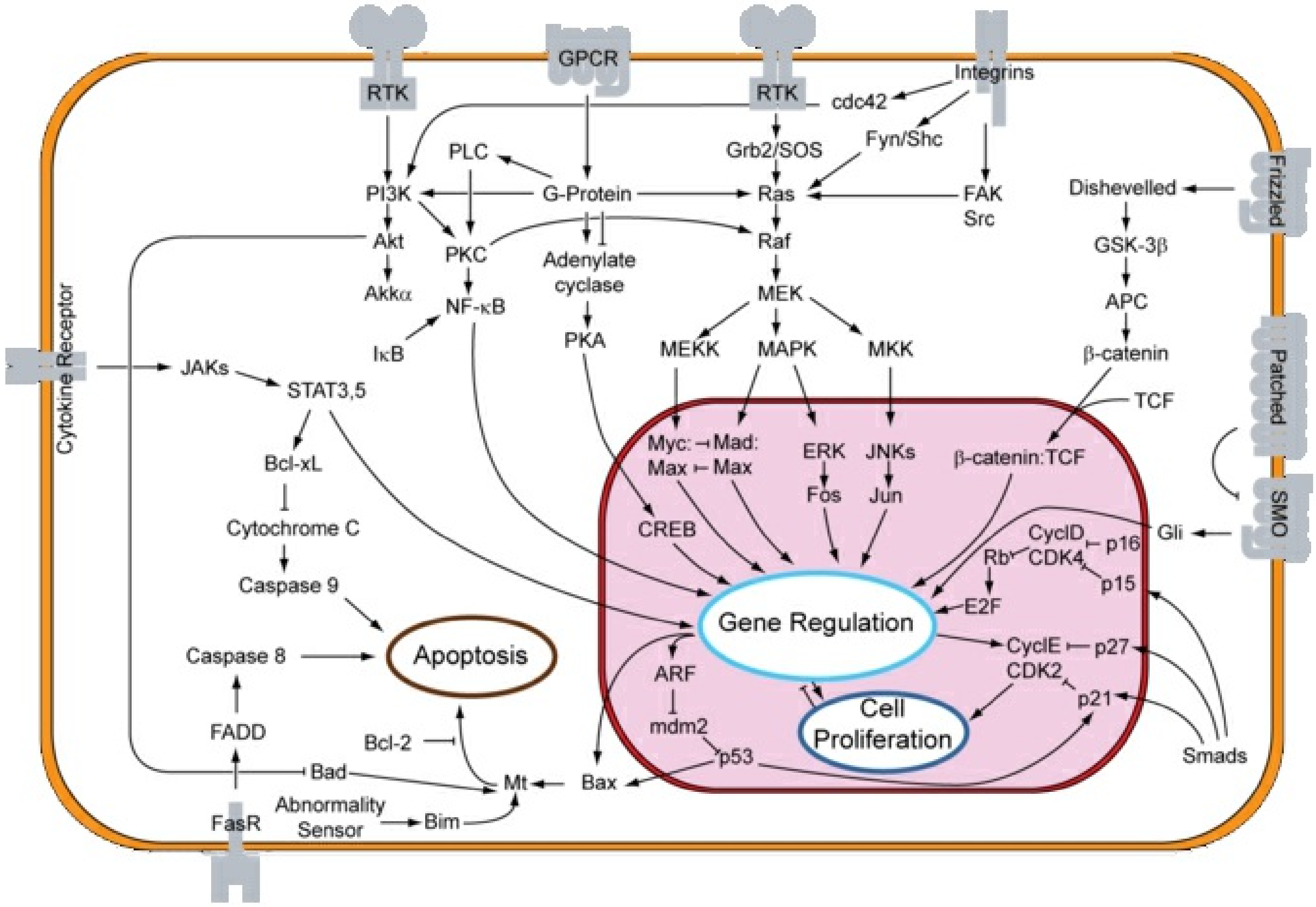
An extracellular signalling molecule, also referred to as a ligand, normally binds to a receptor on the surface of the cell from where it is transmitted into the cell. However, there are also numerous intracellular receptor proteins. Hundreds of signalling molecules are known, including proteins, peptides, amino acids, steroids, retinoids, fatty acid derivatives and dissolved gases such as nitric oxide or carbon monoxide. The majority of signalling molecules are hydrophilic and thus unable to pass through the cell membrane. But there are also some very small signalling molecules that are hydrophobic and can easily diffuse through the cell membrane. Grouped according to function, the signalling molecules include a broad range of different proteins such as hormones, growth factors, components of the extracellular matrix, cytokines, chemokines, neurotransmitters and neurotrophins. Moreover, environmental stimuli such as light, odour, temperature fluctuations and mechanical stimuli can invoke signalling processes.



Using coordinated protein-protein interactions to reach the goal

After a signal is received by a receptor molecule it is transmitted to its target inside the cell – the effector protein. This is achieved through coordinated protein-protein interactions. For example, a signal activates a kinase, which in turn phosphorylates a protein. The thus modified protein activates or inhibits a transcription factor. In many cases, the signals are not transmitted in a linear fashion. A protein, once stimulated by a particular stimulus, might not only have an effect on a single molecule but could also affect a large number of partners. The processing of signals also involves secondary messengers such as cAMP (cyclic adenosine monophosphate), cGMP (cyclic guanosine monophosphate) or Ca2+ (calcium ions). Since these messengers are able to activate different signalling pathways, they often serve as interfaces between different signal transduction pathways. This is why many signal research projects focus specifically on these proteins.

As previously mentioned, there are intracellular receptors as well as a large number of receptors that are anchored in the cell membrane. These membrane-bound proteins expose their binding domain to the extracellular space. One segment is embedded into the membrane and another part extends into the cell’s interior. This enables the receptors to bind their specific signalling molecules outside the cell. The conformation of the receptor changes and the signal is then transmitted into the cell.



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A few signalling pathways fulfil numerous tasks

Ion channels are examples of membrane receptors. They are controlled by ligands or voltage changes and are of decisive importance for the transduction and amplification of neuronal signals. Another important group of receptors is the G protein-bound receptors. The signalling pathways that are controlled by G proteins are the best understood of all signalling pathways. They mediate processes such as vision, smell and the effect of numerous hormones and neurotransmitters. Another important group of receptors controls enzyme-coupled signalling pathways. This group includes receptor tyrosine kinases which activate the MAP kinase pathway and the PI3 kinase signalling pathway, or the tyrosine kinase-coupled receptors such as cytokine receptors which activate the JAK-STAT signalling pathways or receptor-serine/threonine kinases that affect the TGF signalling pathway. The Wnt, Notch and the NF-kappa-b signalling pathways are activated through proteolytic processes occurring at the receptor. Signal transduction is an excellent example of nature's ability to create a huge variability from a few basic constituents. The number of signalling pathways is somewhat small. However, since the cells are able to specifically modulate these signalling pathways, they are able to use them for a broad range of different functions.

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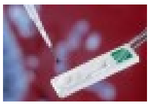

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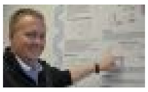

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