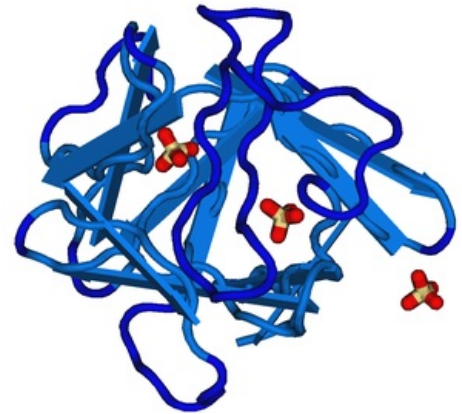


Growth factor

Growth factors are substances (most often of a protein nature) that are produced by various cells of the body and that influence a number of cellular processes such as growth, proliferation, differentiation, survival and maturation of cells or tissues. In addition to these functions, they can also influence cellular metabolism. Growth factors include, for example, platelet-derived growth factor (PDGF), epidermal growth factor (EGF), insulin-like growth factors (IGFs), nerve growth factor (NGF), fibroblast growth factor (FGF), erythropoietin (EPO), thrombopoietin, etc.

Action

Growth factors act as local mediators only in the vicinity of their synthesis site (paracrine action). The responses to them are slow (on the order of hours) and require many intracellular conversion steps that ultimately lead to changes in gene expression. Growth factors often signal through the mitogen-activated protein kinase (MAPK) signalling cascade. This cascade often has a stimulatory effect on the cell cycle.



Fibroblast growth factor

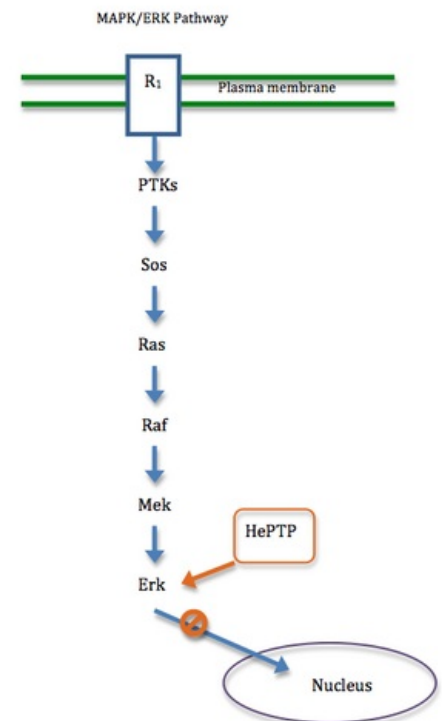
Receptors for growth factors

They are transmembrane proteins with an **extracellular part** that binds growth factors, a **transmembrane part** that penetrates the cytoplasmic membrane, and an **intracellular part** that has tyrosine kinase activity (phosphorylates tyrosines). Binding of a ligand to a receptor causes dimerization with another activated receptor and this leads to a change in protein conformation. The change in conformation activates tyrosine kinase activity and autophosphorylation of tyrosine residues of dimerized receptors occurs. The activated receptor is inactivated after a short time by endocytosis of the receptor with bound growth factor and degradation in the cell.

Growth factor signalling

The activated (phosphorylated) receptor interacts with a number of cytoplasmic proteins. **Ras proteins** are important proteins in growth factor signalling . Ras proteins are GTP-binding proteins and proto-oncogenes that have GTPase activity similar to the α subunit of G-proteins (cleaves bound GTP to GDP + P). The Ras protein does not interact with the activated receptor directly, but via so-called adapter proteins (e.g. Sos, Grb). This interaction results in GDP being released from Ras and GTP binding in its place. The GTP-bound Ras protein is a signalling-active form that enables the binding and activation (by autophosphorylation) of the first of several kinase cascades. This kinase is the **Raf protein**(also called MAPKKK or MAP3K = mitogen-activated protein kinase). The Raf protein transmits the signal in the cell by phosphorylating other protein kinases and the signalling cascade is amplified. Meanwhile, Ras protein is inactivated by the hydrolysis of GTP to GDP and phosphate by the Ras protein itself. Another protein kinase phosphorylated by the Raf protein is **MEK** (MAP and ERK kinase, also called MAPKK or MAP2K = mitogen-activated protein kinase). **Protein kinase MEK** phosphorylates **ERK** (Extracellularly Regulated Kinase, also MAPK = mitogen-activated protein kinase) and after this phosphorylation activation dimerizes and translocates to the cell nucleus, where it phosphorylates transcription factors and thus affects the gene expression of a number of genes (often other transcription factors) .

Summary : growth factor → receptor with its own tyrosine kinase activity → adapter proteins → Ras → Raf → MEK → ERK → cell nucleus → influencing transcription.



The MAPK signalling cascade

Links

Related articles

- Cell signalling
- Cytokines

External links

- Growth factor signalling (<https://www.youtube.com/watch?v=r7GoZ9vFCY8%7C>)

Source

- SVÍGLEROVA, Jitka. *Growth factor* [online]. Last revision 2/18/2009, [cit. 11/12/2010]. <https://web.archive.org/web/20160306065550/http://wiki.lfp-studium.cz/index.php/Růstový_faktor >.
- BRUCE, Alberts, D BRAY and A JOHNSON, et al. *Basics of cell biology*. 1st edition. Ústí nad Labem: Espero Publishing, 1998. 630 pp. ISBN 80-902906-0-4 .
- MATOUŠ, Bohuslav, et al. *Fundamentals of medical chemistry and biochemistry*. 1st edition. Prague: Galén, 2010. 540 pp. ISBN 978-80-7262-702-8 .

Reference

1. BRUCE, Alberts, D BRAY and A JOHNSON, et al. *Basics of cell biology*. 1st edition. Ústí nad Labem: Espero Publishing, 1998. 630 pp. ISBN 80-902906-0-4 .
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