Classes of Growth Factors

A growth factor is a naturally occurring substance capable of stimulating cellular growth, proliferation and differentiation. Growth factors are important for regulating a variety of cellular processes and typically act as signaling molecules between cells. Examples are cytokines and hormones that bind to specific receptors on the surface of their target cells.

Individual growth factor proteins tend to occur as members of larger families of structurally and evolutionarily related proteins. The main families are:

Cytokines are protein molecules secreted by the nervous system and by numerous cells of the immune system and are signaling molecules used extensively in intercellular communication. Cytokines can be classified as proteins, peptides, or glycoproteins; the term "cytokine" encompasses a large and diverse family of regulators produced throughout the body by cells of diverse embryological origin.

Lymphokines are a subset of cytokines that are produced by a type of immune cell known as a lymphocyte.

A **Monokine** is a type of cytokine produced primarily by monocytes and macrophages. Examples include interleukin 1 and tumour necrosis factor-alpha.

Adrenomedullin (AM) AM was initially identified as a vasodilator. Other effects of AM include increasing the tolerance of cells to oxidative stress and hypoxic injury and growing new blood vessels. AM is seen as a positive influence in diseases such as hypertension, myocardial infarction, chronic obstructive pulmonary disease and other cardiovascular diseases, whereas it can harmfully help cancer cells to proliferate.

Angiopoietin (Ang1, Ang2, Ang3, Ang4) promotes the growth of new blood vessels from pre-existing blood vessels. Ang1 and Ang2 are required for the formation of mature blood vessels.

Autocrine motility factor is secreted by cancer cells, where it is called autocrine motility factor and stimulates the spread of a disease from one organ or part to another non-adjacent organ or part.. The same protein is involved in cellular generation and conversion of glucose, while outside the cell it helps spinal and sensory neurons to survive.

Bone morphogenetic proteins (BMPs) Originally discovered by their ability to induce the formation of bone and cartilage, BMPs are now considered to constitute a group of pivotal signals, orchestrating tissue architecture throughout the body. cancerous disease often involves misregulation of the BMP signalling system. Absence of BMP signalling is, for instance, an important factor in the progression of colon cancer and conversely overactivation of BMP signalling following reflux-induced esophagitis provokes Barrett's esophagus and possible later cancer.

Brain-derived neurotrophic factor (BDNF) BDNF acts on certain neurons of the central nervous system and the peripheral nervous system, helping to support the survival of existing neurons, and encourage the growth and differentiation of new neurons and synapses.

C. Reactive protein (CRP) is a protein found in the blood, the levels of which rise in response to inflammation.

Epidermal growth factor (EGF) is a growth factor that plays an important role in the regulation of cell growth, proliferation, and differentiation. It can suppress cancer cells & gastric secretions.

Erythropoietin (EPO) Formed by the kidneys and stimulates red blood cell production.

Fibroblast growth factor (FGF) Stimulates different cell types; cell migration and adhesion protein fibronectin.

Glial cell line-derived neurotrophic factor (GDNF) GDNF is a small protein that is highly important in promoting the survival of many types of neurons.

Granulocyte colony-stimulating factor (G-CSF) is a glycoprotein, growth factor and cytokine produced by a number of different tissues to stimulate the bone marrow to produce granulocytes and stem cells. G-CSF then stimulates the bone marrow to release them into the blood. G-CSF also stimulates the survival, proliferation, differentiation, and function of neutrophil precursors and mature neutrophils.

Granulocyte macrophage colony-stimulating factor (GM-CSF) GM-CSF is a cytokine that stimulates stem cells to produce white blood cells as needed to fight infection.

(Fem) **Growth differentiation factor-9 (GDF9)** GDF9 plays an important role in the development of primary follicles in the ovary. It therefore has a significant role in fertility.

Haemopoietic Growth Factor

Hepatocyte growth factor (HGF) Hepatocyte growth factor regulates cell growth, cell motility, and morphogenesis, the biological process that causes an organism to develop its shape, in an embryo, mature cell or tumour cell.

Immunoglobulins, (Ig) Involved in the immune response: An antibody, also known as an immunoglobulin, is a large Y-shaped protein used by the immune system to identify and neutralize foreign objects such as bacteria and viruses. In mammals there are five antibody isotypes:

IgA - Found in mucosal areas, such as the gut, respiratory tract and urogenital tract, and prevents colonization by pathogens. Also found in saliva, tears, and breast milk.

IgD – Functions mainly as an antigen receptor on B cells that have not been exposed to antigens. It has been shown to activate basophils and mast cells to produce antimicrobial factors.

IgE – Binds to allergens and triggers histamine release from mast cells and basophils, and is involved in allergy. Also protects against parasitic worms.

IgG – its four forms, provides the majority of antibody-based immunity against invading pathogens. The only antibody capable of crossing the placenta to give passive immunity to foetus.

IgM - Eliminates pathogens in the early stages of B cell mediated (humoral) immunity before there is sufficient IgG.

Insulin-like growth factor (IGF1 and 2) Stimulates healthy cell growth

Interferon (IFN–a, IFN–b, IFN –g etc) There are about 10 recognised IFNs and they are all antiviral agents and can fight tumours. They are named after their ability to "interfere" with viral replication within host cells. IFNs have other functions: they activate immune cells, such as natural killer cells and macrophages; they increase recognition of infection or tumour cells by up-regulating antigen presentation to T lymphocytes; and they increase the ability of uninfected host cells to resist new infection by virus. Certain host symptoms, such as aching muscles and fever, are related to the production of IFNs during infection.

Interleukines (IL)

IL-1- Cofactor for IL-3 and IL-6. Activates T cells.
IL-2- T-cell growth factor. Stimulates IL-1 synthesis. Activates B-cells and NK cells.
IL-3- Stimulates production of all non-lymphoid cells.
IL-4- Growth factor for activated B cells, resting T cells, and mast cells.
IL-5- Induces differentiation of activated B cells and eosinophils.
IL-6- Stimulates Ig synthesis. Growth factor for plasma cells.
IL-7- Growth factor for pre-B cells.
IL- 8, to IL-35 etc.

Migration-stimulating factor

Myostatin or Growth Differentiation Factor 8 (GDF-8) inhibits muscle differentiation and growth.

Nerve growth factor (NGF) Stimulates embryonic ganglia; maintains SNS; Aids mature nerve cells.

Neurotrophin-3 (NT-3) and Neurotrophin-4 (NT-4), Neurotrophins are a family of proteins that induce the survival, development, and function of neurons.

Placental growth factor (PlGF)

Platelet-derived growth factor (PDGF) Stimulates different cell types; wound healing; may contribute to atherosclerosis.

Transforming growth factor alpha (TGF-α) TGFα stimulates the proliferation of neural cells in the adult injured brain and induces epithelial development. It is overactive in some human cancers. It is closely related to EGF, and can also bind to the EGF receptor with similar effects .

Transforming growth factor beta (TGF-β) is a protein that controls proliferation, cellular differentiation, and other functions in most cells. It plays a role in immunity, cancer, heart disease, diabetes, Marfan syndrome, and Loeys–Dietz syndrome.

Tumour angiogenesis factors Produced by normal and tumour cells; stimulates growth of new capillaries, organ regeneration and wound healing.

Tumour necrosis factor-alpha (TNF-α) or **Tumour necrosis factor beta (TNF-β)** is a cytokine involved in systemic inflammation. The primary role of TNF is in the regulation of immune cells. Dysregulation of TNF production has been implicated in a variety of human diseases, including Alzheimer's disease, cancer, major depression,and inflammatory bowel disease (IBD).

Vascular endothelial growth factor (VEGF) is active in the growth of new blood vessels, lymphatic vessels and the growth and survival of endothelial cells that line the entire circulatory system, from the heart to the smallest capillary and it can also affect the permeability of blood vessels.

Wnt Signaling Pathway The Wnt signaling pathway is a network of proteins best known for their roles in the formation and development of an embryo and is also involved in normal physiological processes in adult animals. Inappropriate signalling is involved in the formation and development of cancer.

