SPECIFIC GROWTH FACTORS INDUCE PANCREATIC PARENCHYMAL CELLS

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Relevance. The growth factor is a collective term of mitogenic peptide hormones that promote receptor-mediated proliferation and cell differentiation and motility. In the latter case, a cell can only divide by mitosis after first having broken off contact with adjacent cells under the influence of a scatter factor [10]. Cell proliferation can be triggered by many chemical mediators, such as growth factors, hormones, and cytokines. Although hormones and many cytokines are involved in the stimulation or inhibition of cell growth, they have many other functions. Signals from the extracellular matrix are also important inducers of cell replication. In this section, we focus on polypeptide growth factors, whose main role is to promote cell survival and proliferation and are important in regeneration and healing [4]. expansion of cell populations usually involves an increase in cell size (growth), cell division (mitosis), and protection from apoptotic death (survival). Strictly speaking, the term "growth factors" should be used for proteins that increase cell size, and "mitogens" and "survival factor" should be used for molecules with the other activities. However, many growth factors have all these activities, and by convention "growth factor" is used for a protein that expands cell populations by stimulating cell division (usually accompanied by increased cell size) and by promoting cell survival. Most growth factors have pleiotropic effects; that is, in addition to stimulating cellular proliferation, they stimulate migration, differentiation, and contractility, and enhance the synthesis of specialized proteins (such as collagen in fibroblasts). A growth factor may act on a specific cell type or multiple cell types. They induce cell proliferation by binding to specific receptors and affecting the expression of genes whose products typically have several functions they relieve blocks on cell cycle progression (thus promoting replication), they prevent apoptosis, and they enhance the synthesis of cellular proteins in preparation for mitosis. A major activity of growth factors is to stimulate the function of growth control genes, many of which are called proto-oncogenes because mutations in them lead to the unrestrained cell proliferation characteristic of cancer (oncogenesis). Some growth factors stimulate the proliferation of some cells and inhibit the cycling of other cells. A growth factor can have opposite effects on the same cell depending on its concentration. An example of such a growth factor is transforming growth factor-β (TGF-β). There is a huge (and ever-increasing) list of known growth factors. Rather than attempt exhaustive cataloging, we will highlight only

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selected molecules that contribute to parenchymal cell proliferation. Many growth factors are produced by parenchymal cells or stromal cells (connective tissue) in response to cell injury or loss. Other growth factors involved in repair are produced by leukocytes that are recruited to the site of injury or are activated at this site, as part of the inflammatory process. In the following, we discuss specific principles of how these growth factors work. Several clinical studies are done to identify the involved mechanisms in parenchymal cell proliferation and differentiation however there is no single study that clarified the underlying molecular mechanisms that stand behind it in particular the growth factors mechanisms and effects on parenchymal cells of the brain and heart. Cell proliferation physiology: cell proliferation occurs in these stages: signal reception: a ligand (growth factor) binds to "its" receptor on the cell membrane. Signal transduction: limited activation of growth factor receptors activates signal-transducing proteins on the inside of the cell membrane (mitogen-activated protein kinase cascade). Signal transmission: the proliferation signal is passed to the cell nucleus by cytoplasmic second messenger substances. Signal implementation: induction and activation of nuclear regulatory factors initiate DNA transcription, resulting in cell division. The individual steps in proliferation are regulated by cell contact mechanisms (selectins, cadherins, integrins) and proliferation stimulators (proto-oncogene "c-onc", growth factors), inhibitors (TGF-β and TGF-α, p53, RB1, and WT1), and modulators (Homeobox Genes).

Growth factors are produced by autocrine secretion (physiologically; during embryogenesis and tissue regeneration, pathologically; continuous autocrine secretion occurs in tumor growth) or paracrine secretion (typical type of growth factor secretion).

Growth factors participate in the migration starting signal for cell migration. IGF-22 controls the initiation of the cell cycle. The WT-1 gene product inhibits mitogen1 transcription. In this manner, it promotes differentiation of the embryonic primordium of the kidney and inhibits adjacent genes, such as IGF-22, which control the initiation of the cell cycle. On the other hand, the WT-2 gene regulates cell proliferation.

Obojectives: assess the role and potential mechanism of growth factor in modulating beta cell ability for regeneration and improving already impaired beta cells.

Materials and methods. We searched PubMed and Scopus, and we took the most recent studies and findings on the issue. We use these terms "growth factor in beta cell regeneration", "growth factors in pancreas regeneration". Results were excluded by title and then abstract irrelevance. The final results were 15 and due to the limit in the number of the required references we minimize them to only 10 papers.

Results and their discussions. Transforming growth factors, insulin and insulin-like growth factors are involved in the regulation of α and β cells [5, 8].

Neuronal growth factors(NGF) are released from postsynaptic innervated cells and via retrograde axonal transport transferred to the damaged presynaptic cell to repair the injured axon [9].

Cardioprotective growth factors are intended to protect the heart from acute ischemia and reperfusion injuries [3]. Cardiac regeneration is a broad process that involves biomolecules, including angiogenesis, extracellular matrix remodeling, cardiomyocyte proliferation, and stem cell recruitment [6].

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Fibroblast growth factors in lung cancer cells (FGF, TGF, and EGF) [7]. Protein phosphorylation cascades play a key role in transmitting growth signals. The receptor-binding site for peptide/protein growth factors is on the outer surface of the cell membrane, in other words, the extracellular domain. Most cell surface receptors for growth factors show tyrosine kinase activity, meaning that they put a phosphate group on a downstream protein tyrosine residue. When activated by binding of TGF-beta cytokines, this receptor can phosphorylate downstream proteins on serine and threonine residues. "Downstream" here means an event triggered after TGF-beta binding to its receptor [1, 2, 7].

Conclusions: physiologically, cells pass to mitosis and hyperplasia only under decompensated hypertrophy. Therefore, protooncogenes are obligatory for this process. Where the growth factors' role takes place in this process and how? Growth factors are usually are stimulatory signals from specific activatory transcription factors that lead to increased transcription of specific DNA sequences. The resulting protein will trigger DNA replication and or phosphorylation of specific protooncogenes that, in turn initiate the mitosis process and transfer the cell to a new stage of its life cycle. While this regulated mitosis can be of use in stimulating many dormant adult stem cells or the already matured cells in the vital organs with a permanent capacity for mitosis to divide and later on stimulate differentiation.

The clinical importance of growth factors appears in their ability to recruit them as therapeutic agents to cure many parenchymal damage to the permanent and labile types of tissue. In addition, they can be a therapeutic target for new medications. Therefore, growth factors hold a promising future for our health in the upcoming years.

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