BIOLOGICAL FUNCTIONS OF ANGIOGENIN

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Annotatsiya. Angiogenez — bu embrional rivojlanish, to‘qimalarning o‘sishi, jarohatlarning bitishi va regeneratsiya jarayonlarida muhim rol o‘ynaydigan asosiy biologik jarayondir. Shuningdek, u gipoksiya va ishemiya bilan bog‘liq turli patologik holatlarda, jumladan, saraton, yurak-qon tomir kasalliklari va yallig‘lanish kasalliklarida muhim ahamiyatga ega. Aniqlangan ko‘plab angiogenik omillar orasida angiogenin eng kuchli va biologik jihatdan muhim angiogenez regulyatori hisoblanadi. Angiogenin — ribonukleaza superoilasiga mansub kichik, sekretsiyalanuvchi oqsil bo‘lib, endoteliya hujayralarining proliferatsiyasi, migratsiyasi va neovaskulyarizatsiyasini rag‘batlantira oladi. Ushbu maqola angiogeninning molekulyar tuzilishi, biologik funksiyalari, harakat mexanizmlari va fiziologik hamda patologik angiogenezdagi klinik ahamiyatini keng qamrovli tarzda ko‘rib chiqadi. Angiogeninning rolini chuqur tushunish regenerativ tibbiyot va onkologiyada yangi diagnostik biomarkerlar va terapevtik strategiyalarni ishlab chiqishga yordam berishi mumkin.

Kalit so‘zlar: angiogenez, angiogenin, neovaskulyarizatsiya, gipoksiya, endoteliya hujayralari

Аннотация. Ангиогенез — это фундаментальный биологический процесс, играющий ключевую роль в эмбриональном развитии, росте тканей, заживлении ран и регенерации. Он также участвует в различных патологических состояниях, связанных с гипоксией и ишемией, включая рак, сердечно-сосудистые заболевания и воспалительные расстройства. Среди множества идентифицированных ангиогенных факторов, ангиогенин считается одним из самых мощных и биологически значимых регуляторов ангиогенеза. Ангиогенин — это небольшая секретируемая белковая молекула из суперсемейства рибонуклеаз, способная стимулировать пролиферацию, миграцию эндотелиальных клеток и неоваскуляризацию. В данной статье представлен всесторонний обзор молекулярной структуры, биологических функций, механизмов действия и клинического значения ангиогенина в физиологическом и патологическом ангиогенезе. Глубокое понимание роли ангиогенина может способствовать разработке новых диагностических биомаркеров и терапевтических стратегий в регенеративной медицине и онкологии.

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Ключевые слова: ангиогенез, ангиогенин, неоваскуляризация, гипоксия, эндотелиальные клетки

Abstract. Angiogenesis is a fundamental biological process that plays a critical role in embryonic development, tissue growth, wound healing, and regeneration. It is also involved in various pathological conditions associated with hypoxia and ischemia, including cancer, cardiovascular diseases, and inflammatory disorders. Among the numerous angiogenic factors identified to date, angiogenin is considered one of the most potent and biologically significant regulators of angiogenesis. Angiogenin is a small, secreted protein belonging to the ribonuclease superfamily and is capable of stimulating endothelial cell proliferation, migration, and neovascularization. This article provides a comprehensive review of the molecular structure, biological functions, mechanisms of action, and clinical significance of angiogenin in both physiological and pathological angiogenesis. Understanding the role of angiogenin may contribute to the development of novel diagnostic biomarkers and therapeutic strategies in regenerative medicine and oncology.

Keywords: angiogenesis, angiogenin, neovascularization, hypoxia, endothelial cells

INTRODUCTION

Angiogenesis refers to the formation of new blood vessels from pre-existing vasculature and is essential for normal growth, development, and tissue repair. This complex and tightly regulated process involves endothelial cell activation, proliferation, migration, and differentiation. Physiological angiogenesis occurs during embryogenesis, postnatal growth, and wound healing, whereas pathological angiogenesis is associated with diseases such as cancer, diabetic complications, rheumatoid arthritis, and ischemic cardiovascular disorders.

The regulation of angiogenesis depends on a dynamic balance between pro-angiogenic and anti-angiogenic factors. Disruption of this balance leads to either excessive or insufficient vascular growth. In recent decades, significant attention has been directed toward identifying key molecular regulators involved in angiogenesis. Among these regulators, angiogenin has emerged as a critical mediator due to its strong angiogenic activity and unique molecular properties.

Angiogenin was initially isolated from conditioned media of human adenocarcinoma cells and later identified in normal human plasma and various tissues. Its expression is particularly high in the liver and increases under conditions of cellular stress, hypoxia, and tissue injury. These findings suggest that angiogenin plays an important role in adaptive and protective responses of the organism.

MATERIALS AND METHODS

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This study is based on a comprehensive review of published scientific literature related to angiogenin and angiogenesis. Peer-reviewed articles, review papers, and experimental studies indexed in international scientific databases such as PubMed, Scopus, and Web of Science were analyzed. The selection criteria included studies focusing on the molecular structure, biological activity, signaling mechanisms, and clinical relevance of angiogenin.

Data from in vitro, in vivo, and clinical studies were systematically evaluated to summarize current knowledge regarding angiogenin-mediated angiogenesis. Particular attention was paid to studies describing the interaction of angiogenin with endothelial cells, its nuclear translocation, and its role in ribosomal RNA transcription.

RESULTS

Angiogenin is a single-chain polypeptide consisting of 123 amino acids and belongs to the ribonuclease A superfamily. Sequence analysis reveals approximately 33% homology with pancreatic ribonuclease A; however, angiogenin exhibits distinct structural and functional characteristics. Its ribonucleolytic activity is relatively weak but is essential for its angiogenic function.

Experimental studies have demonstrated that angiogenin stimulates endothelial cell proliferation and migration, which are key steps in the formation of new blood vessels. One of the most important mechanisms underlying its angiogenic activity is its ability to translocate into the nucleus of endothelial cells. Once inside the nucleus, angiogenin binds to DNA and enhances ribosomal RNA transcription, leading to increased protein synthesis and cell growth.

In addition, angiogenin promotes degradation of the extracellular matrix by activating proteolytic enzymes, facilitating endothelial cell invasion and capillary tube formation. Studies on ontogenetic expression patterns indicate that angiogenin is predominantly synthesized in the liver and is upregulated during tissue regeneration and stress conditions.

DISCUSSION

The results of numerous studies confirm that angiogenin is a central regulator of angiogenesis under both physiological and pathological conditions. Hypoxia is one of the strongest inducers of angiogenin expression. Under low oxygen conditions, hypoxia-inducible factors (HIF-1α and HIF-2α) activate transcription of angiogenin, thereby promoting neovascularization and improving tissue oxygenation.

The nuclear translocation of angiogenin represents a unique mechanism among angiogenic factors and highlights its dual role as both a signaling molecule

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and a regulator of gene expression. Inhibition of angiogenin nuclear import has been shown to significantly reduce angiogenesis, further emphasizing its importance in endothelial cell biology.

Clinically, elevated levels of angiogenin have been detected in various diseases, including cancer, ischemic heart disease, and inflammatory disorders. These findings suggest that angiogenin may serve as a valuable biomarker for disease progression and therapeutic response. Moreover, modulation of angiogenin activity holds promise for the development of novel therapeutic approaches aimed at enhancing or inhibiting angiogenesis, depending on the clinical context.

CONCLUSION

Angiogenin is a powerful angiogenic factor that plays a crucial role in the regulation of blood vessel formation. Its unique molecular structure, ability to translocate into the nucleus, and involvement in ribosomal RNA transcription distinguish it from other angiogenic regulators. Further investigation of angiogenin-mediated signaling pathways may provide new insights into the mechanisms of angiogenesis and lead to innovative diagnostic and therapeutic strategies in regenerative medicine, oncology, and cardiovascular diseases.

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