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The Role and Research Progress of C1QBP in Tumors

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ABSTRACT
Complement C1q binding protein (C1QBP) is one of the multifunctional acidic proteins with multiple compartments. It exhibits basic characteristics of universal expression and evolutionary conservation. C1QBP plays a crucial role in various biological processes, such as ensuring mitochondrial functional homeostasis, energy metabolism, cancer, infection, inflammatory response, etc. C1QBP is closely associated to the occurrence of tumors and exhibits differential expression in various types of cancer. At the same time, the expression pattern of C1QBP shows tissue specificity in regulating tumor progression. In addition, C1QBP is significantly correlated with drug resistance and patient prognosis, making it a biological marker for predicting tumor progression. This article mainly analyzes the specific mechanism of action of C1QBP in tumors, hoping to provide guidance for clinical prevention and treatment of tumors.

KEYWORDS
C1QBP; Tumor; Mechanism

1 Introduction

The microenvironment of tumor cells directly affects its growth and development. Hyaluronic acid is a key component of the extracellular matrix. For most malignant tumor patients, the expression of hyaluronic acid and most hyaluronic acid mucin family proteins is significantly elevated, and C1QBP is a biomarker of tumor progression [1]. C1QBP plays a crucial role in the process of tumor occurrence. In various type of malignant tumors, C1QBP exhibits abnormal expression. In tumor tissues such as glioma, prostate cancer, ovarian cancer, breast cancer, endometrial cancer, thyroid cancer, colorectal cancer, C1QBP shows increased activity or expression. The risk of tumor recurrence, tumor Gleason score, pathological grade are positively correlated with C1QBP protein content [2]. Therefore ,C1QBP plays a significant role in various cancers. This article reviews the role and research progress of C1QBP in tumors.

2 Structural of C1QBP

Complement C1q binding protein (C1QBP), also known as hyaluronic acid binding protein 1 (HABP1), globular head domain complement 1q (gC1qR) and P32, is a globular protein that interacts with complement component C1q. As one of the mitochondrial matrix proteins, C1QBP is mainly localized in mitochondria, but it can also be detected in various nuclei, cell surfaces, and cell compartments [3]. C1QBP consist of 5 introns and 6 exons, with the gene located on chromosome 17p13.3. The protein has a molecular weight of 33kDa and is encoded by 282 amino acid residues. For the immature C1QBP protein, its N-terminus contains a 1 to 73 amino acids segment with a mitochondrial localization sequence, Through post-translational modification and enzymatic cleavage of the initial N-terminal mitochondrial targeting sequence, mature C1QBP protein is formed and translocated to the cell surface. C1QBP is a non covalent trimer composed of three specific peptide chains A, B, and C. The three monomers form a circular quaternary structure, exhibiting asymmetric charge distribution on the surface around the central channel [4]. C1QBP is a highly charged acidic molecule with three N-glycosylation sites. The multiple forms of C1QBP significantly enhance its affinity for ligand binding.

3 Functional of C1QBP

C1QBP is one of the multifunctional proteins, which can not only regulate nuclear greening and cell apoptosis, participate in energy metabolism, maintain good activity and homeostasis of mitochondrial, but also participate in pre-mRNA indirect, promote ribosome synthesis, and participate in infection and inflammatory reactions, etc [5]. C1QBP is significantly correlated with the occurrence of tumors, and its role varies depending on the type of tumor. Its expression differs across different tumors, exhibiting obvious tumor specificity.

3.1 DNA damage repair

In maintaining genomic stability, the Mre11/Rad50/NBS1 complex plays a crucial role, and C1QBP controls the

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assembly and activation of the Mre11/Rad50/NBS1 complex, maintaining the stability of the genomic Mre11 nuclease, thereby effectively repairing damaged DNA and facilitating homologous recombination [6]. For patients with breast cancer, effective inhibition of C1QBP can promote tumor regression after chemotherapy. This demonstrates critical role of C1QBP in repairing damaged DNA, and it could become a new target for clinical treatment of cancer.

3.2 Participate in the generation of ribosomes

In the synthesis of intracellular proteins, ribosomes are one of the indispensable substances. The composition of mammalian ribosomes includes 40S subunits and 60S subunits. In the early stages of mammalian ribosome biogenesis, the role of C1QBP is crucial [7]. Between the pre-60S particles and the pre-40S particles, fibrin interacts with C1QBP to form a bridge. Human nucleolar protein Nop52 can effectively inhibit the bridging effect of C1QBP, promote 90S division, and further form ribosomal subunit 60S and 40S [8]. In addition, C1QBP can also promote the formation of ribosomes in yeast and plays a very crucial role in assembling mitochondrial ribosomes; Thus, in is evident that C1QBP palys a crucial role in promoting ribosome synthesis.

3.3 Ensure the morphology of endoplasmic reticulum and mitochondria remains normal

The dynamic recombination of cellular netwolks and structures is strictly regulateed by mitochondrial fusion protein 1 (Mfn1), mitochondrial endogenous motor protein (Opa1), and motor protein related protein 1 (Drp1), which not only directly affects the regulation and metabolism of cell death, but also closely related to mitochondrial fission and fusion mechanisms [9]. C1QBP is a mitochondrial proteins. In cervical cancer patients, overexpression of C1QBP in Hela cells can lead to a significant increase in mitochondrial fibrils. If C1QBP is knocked down, it can significantly enhance mitochondrial punctation and fragmentation. This shows that C1QBP plays a crucial role in mitochondrial fusion and fission [10]. Mitochondrial fission plays a crucial role in the process of eliminating damaged or aging mitochondria and promoting the generation of new mitochondria. Ultrastructural analysis reveals that inhibiting C1QBP leads to abnormal mitochondrial structure with more punctate endoplasmic reticulum and fewer fragmented or/and fragmented cristae [11]. The significant dissociation of its ribosomes indicates that the expression level of C1QBP has a direct impact on the normal morphology of the endoplasmic reticulum and mitochondria in cells. C1QBP can effectively regulate the expression of respiratory chain complexes encoded by mitochondrial DNA, thereby maintaining mitochondrial integrity.

4 The role of C1QBP in tumors

4.1 C1QBP promotes tumor cell metastasis and chemotaxis

C1QBP can effectively activate epidermal growth factor mediated by receptor tyrosine kinase to promote distant metastasis and chemotaxis of tumor cells，further causing breast cancer [12]. Once epidermal growth factors are present in the body, protein kinase interacts with C1QBP, activates protein kinase, promotes its translocation, and uses filamentous protein to promote the effective polymerization of actin, so as to achieve cell chemotaxis. Turthermore, in breast cancer patients, C1QBP is overexpressed in cancer cell tissues, and TNM staging, distant metastasis and C1QBP expression level have significant correlation. As a new regulator, measuring C1QBP expression in cancer tissues can accurately predict effective cancer metastasis, and can serve as a new target for clinical treatment [13]. Through the above analysis, it is found that C1QBP can regulate the signaling pathway, thereby regulating the metastasis and chemotaxis of cancer cells, leading to further cancer progression.

4.2 C1QBP and cell apoptosis, autophagy

Once the growth signal transduction within the cell exceeds energy availability, mitochondria will release a large amount of cytochrome C, leading to cell death and activation of the intrinsic apoptotic pathway. Autophagy, as a pathway that replaces cell death, may be effective in combating cancer cells when they undergo apoptosis and are damaged [14]. P19ARF, PTEN, p53, and Beclin 1, which regulate autophagy, can also be used as tumor suppressor factors. If autophagy inducers are overexpressed, they can reduce cancer levels to some extent or cause autophagic death [15]. The accumulation of C1QBP in mitochondria promotes the production of a large amount of reactive oxygen species, increases the influx of calcium ions into the mitochondria, reduces membrane potential, and further leads to mitochondrial dysfunction.

4.3 C1QBP promotes adhesion and proliferation of tumor cells

Ror patients with renal cell carcinima(RCC), the low expression of C1QBP in their tissue specimens inhibits the progression of RCC. Inhibition of C1QBP expression not only effectively activates Wnt pathway related proteins, but also upregulates LICAM, significantly enhancing the adhesion ability of cancer cells. The mechanism of C1QBP inhibition in RCC has been described in detail [16]. From this, it can be seen that the role of C1QBP is very important in the occurrence and development of RCC. It can serve as a novel biomarker for diagnosing RCC and evaluating its prognosis, and can also

become a new target for predicting prognosis and clinical treatment.

4.4 C1QBP promotes the migration and invasion of tumor cells

As a member of the cold shock protein superfamily, Y-box binding protein 1(YBP1) is significantly correlated with the occurrence of malignant tumors and sreves as one of most indicative biomarker of malignant tumors. Its nuclear localization can clarify the progression of malignant tumors, with poor prognosis and shortened survival [17]. C1QBP can interact with YBP1, negatively regulating tis activation, altering its nuclear translocation and phosphorylation, and thus effectively controlling the activation of YBP1. It is responsible for regulating AR/MP9 signaling, thereby regulating the invasion and migration of tumor cells. In renal cancer patients, C1QBP shows low expression, so the nuclear expression of YBP1 and C1QBP expression can serve as independent factors for predicting disease progression in renal cancer patients.

5 Summary

C1QBP is an evolutionarily conserved multifunctional protein exhibiting pleiotropy. In tumors, C1QBP plays crucial role and is closely associated with processes such as cell chemotaxis, adhesion, metastasis, invasion, apoptosis, and proliferation. C1QBP can serve as a potential target for clinical treatment of malignant tumors. In-depth research on its molecular mechanisms and biological basis in tumors can provide new pathways and targets for clinical treatment of tumors.

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