

Mini review: the relationship between inflammasome and colon cancer

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Abstract: Colon cancer is a common malignant tumor of the digestive system. In the world, the incidence and mortality of colorectal cancer rank the third among malignant tumors. Although there have been great advances in the technical means of this treatment in recent years, the mortality rate continues to rise. Studies have shown that inflammasomes are an important type of polyprotein complex in the innate immune system, which play an important role in identifying and eliminating intestinal pathogens and maintaining intestinal homeostasis. Their abnormal functions are involved in inflammatory bowel disease. And its carcinogenesis. The inflammasome is the central link of the inflammatory response, which is of great significance in the study of many functions and related mechanisms in colon cancer.

Keywords: inflammasome, colon cancer, NLRP3

1. Introduction

Colon cancer is currently one of the most common malignant tumors of the digestive tract. So far, the global incidence of colon cancer has been on the rise. Colitis-related carcinogenesis is one of the main complications of inflammatory bowel disease, and the inflammasome is the main link in the inflammatory response. It plays an important role in maintaining intestinal homeostasis. Its functional variation is involved in the occurrence of carcinogenesis. Therefore, it is of great significance in the study of many functions and related mechanisms of colon cancer.

2. Inflammasome and colon cancer

2.1 Colon cancer

Cancer is one of the main causes of death in our country, among which breast cancer, colorectal cancer and lung cancer rank the top 3 among them. Colon cancer is a common clinical malignant tumor of the digestive tract that occurs in the colon. With the changes in people's lives, the number of colon cancer patients is increasing, and the incidence and mortality of colon cancer are getting higher and higher, generally increasing rapidly after the age of thirty-five, and reaching a peak after the age of eighty [1].

2.2 Inflammasome

Inflammation is the body's immune response against the invasion of external pathogens and various physical and chemical damages. Uncontrolled inflammation is considered to be one of the signs of tumor initiation and progression. The inflammasome is an important part of the inflammatory response, which is crucial to the occurrence of the inflammatory response. The inflammasome is a polyprotein complex composed of three proteins, receptor protein, connexin, and effector protein. When the body is stimulated by a variety of internal and external signals, a series of reactions will occur, making the activation of inflammasomes highly dynamic and orderly [2].

2.3 Inflammatory bodies and colon cancer

Studies have suggested that the occurrence of colorectal cancer (CRC) is related to inflammatory bowel disease. Therefore, there are more and more studies on the relationship between inflammation and CRC, but the results are still controversial. Studies have shown that the effect of NLRP3 inflammasomes on inflammatory bowel disease and CRC is mainly through the regulation of interleukin-1 β (IL-1 β) and

IL-18 [3]. Inflammasomes can induce colon cancer cells to undergo epithelial interstitial transformation and promote their metastasis. Studies have shown that abnormal inflammasome activation is related to a variety of human congenital and acquired inflammatory diseases, and is in maintaining intestinal homeostasis and intestinal carcinogenesis. It plays an important role in the process. It is a type of multi-protein complex composed of intracellular PRRs (intracellular pattern recognition receptors), which can be activated under pathogen infection or abnormal conditions, regulate caspase-1 activity, and trigger pro-inflammatory Factors such as IL-1 β mature and participate in innate immune defense [4].

3. Inflammatory body NLRP3

3.1 Introduction of inflammasome NLRP3

NLRP3 inflammasome is a multi-protein complex and an important part of the innate immune system. It can identify pathogens and cell damage, induce the secretion of inflammatory factors IL-1 β and IL-18, mediate cell pyrolysis, and regulate the body's Inflammation signaling pathway [5]. NLRP3 is the most characteristic and most studied inflammasome. It is mainly expressed in the cytoplasm of monocytes, macrophages, granulocytes, dendritic cells, epithelial cells and osteoblasts. Under the action of inflammation, infection and endogenous stimuli, the expression of NLRP3 is up-regulated [6].

3.2 Activation of inflammasome NLRP3

NLRP3 inflammasome is currently the most in-depth study of inflammasomes, which can be activated by a variety of pathogens and their components or products, such as *Staphylococcus aureus*, *Listeria*, *Candida albicans*, etc.; endogenous damage signals or environment Pathogenic factors, such as extracellular ATP, sodium urate crystal silica, ultraviolet rays, etc. can also activate NLRP3 inflammasome. There are currently four hypotheses about the activation mechanism of NLRP3 inflammasome. They are K⁺ efflux, cathepsin release, reactive oxygen species (ROS) production, mitochondrial damage and dysfunction. However, studies have shown that none of these hypotheses can perfectly explain the activation process of the inflammasome [7].

Some researchers discovered another activation pathway. They used mass spectrometry to identify the phosphorylation modification of serine at position 194 of the NLRP3 protein, and then found that the phosphorylation modification at this site specifically occurs in the priming stage of inflammasome activation. [8].

3.3 Inflammasome NLRP3 and tumors

Inflammasome is a multimeric protein platform that induces pro-caspase-1 activation and inflammatory cytokine maturation in the innate immune system. In addition to being related to autoimmune diseases, the overexpression of IL-1 β may also lead to the occurrence of tumors. Several inflammasomes, including NLRP3, NLRP6, NLRC4, NLRP1 and AIM2, may play a pathogenic role in tumorigenesis by regulating innate and acquired immunity, apoptosis, differentiation and intestinal microbes. The role of NLRP3 in tumor progression is very complex. Studies have shown that in various cancers, NLRP3 has both a cancer-promoting effect and an anti-tumor effect [9].

Studies have shown that the effect of NLRP1 inflammasomes on inflammatory bowel disease and CRC is mainly through the regulation of IL-1 β and IL-18. IL-1 β can promote the growth of CRC cells through the IL-1 β /NF- κ B/mir-181a/ PTEN signaling pathway, and can also induce the production of COX-2, the inflammatory mediator in fibroblasts, which is beneficial to the proliferation and invasion of CRC cells. However, IL-18 mainly plays an inhibitory role in the occurrence of CRC [10].

4. Current research on inflammasome

Some scholars are studying the progress of NLRP3 inflammasomes in infectious diseases. They said that NLRP3 inflammasomes are involved in the occurrence and development of multi-system infectious diseases and are affected by multiple factors. Therefore, they may be specific as early treatment markers for specific pathogen infections. It is relatively low, and routine clinical application is difficult and challenging.

5. Prospects

At present, there are many drug studies that target the intervention of NLRP3 inflammasomes. Among them, the potential value of Chinese patent medicines is relatively high, but they are limited to basic research and have not been promoted in clinical applications. If progress can be made in the research of NLRP3 inflammasomes in the future, Will help to further clarify the role and molecular mechanism of NLRP3 inflammasome in the body, provide new targets for the development of a new generation of drugs, and provide new ideas for the clinical prevention and treatment of cardiovascular diseases and colon cancer.

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