Molecular Mechanism of Carcinogenesis in Laterally Spreading Colorectal Tumors

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Abstract: Colorectal laterally spreading tumor is a superficial tumor of the large intestine with a unique growth pattern and lesion morphology, which has a high potential for carcinogenesis and seriously threatens human health. In recent years, with the rapid development of molecular biology technology, people have a deeper understanding of the molecular mechanism of LST carcinogenesis. The molecular mechanism of LST carcinogenesis includes gene mutation, abnormal signal transduction pathways, and changes in protein interaction networks. Therefore, it is important to explore the molecular mechanism of carcinogenesis in LST to reveal the pathogenesis of colorectal cancer and improve the diagnosis and treatment.

***Keywords*:** colorectal; laterally developing type; tumor carcinogenesis; molecular mechanisms

1. Introduction

Colorectal malignancy is one of the most common malignancies and is one of the leading causes of cancer-related deaths worldwide, and colonoscopy is effective in screening and preventing colorectal cancer. Lateral colorectal tumors (LSTs) are closely related to the occurrence and development of colorectal cancer. Colorectal laterally spreading tumors are special flat lesions larger than 1 cm in diameter, which grow laterally along the superficial or circumferential intestinal wall and less vertically into the deep part of the intestinal wall, and have been called creeping tumors or nodular aggregation tumors because of their morphological appearance. Therefore, in the process of clinical diagnosis, it is important to improve the accuracy of preoperative diagnosis of LSTs to determine the treatment plan for patients with colorectal laterally developing tumors, improve the long-term prognosis of patients, and improve the quality of life of patients.

2. Overview of colorectal laterally spreading tumors

2.1 Classification and clinical characteristics of LSTs

LSTs, or laterally spreading colorectal tumors, can be meticulously divided according to their morphology and growth characteristics. One type is granular with granular proliferation on its surface, like paving stones, while the other is non-granular with a relatively flat or slightly depressed surface, like depressed or mixed. Clinically, LSTs tend to be bulky, but grow inside the intestinal lumen and less frequently invade the deep layers of the intestinal wall. This particular mode of growth may lead to inconspicuous early symptoms, increasing the difficulty of diagnosis. However, as the disease progresses, patients may experience symptoms such as hematochezia and abdominal pain, which need to be highly valued [1].

2.2 Growth pattern and pathological features of LSTs

LSTs, or laterally developing tumors of the colorectum (Figure 1), grow in a unique manner and extend laterally mainly along the mucosal surface of the intestinal wall rather than vertically deep into the intestinal lumen. This mode of expansion makes LSTs potentially more hidden and imperceptible at the initial stage. Pathologically, LSTs may contain an adenomatous component and carry a risk of carcinogenesis. Its surface may be covered with granular or non-granular mucosa with diverse morphologies, including flat, elevated, and depressed, which make LSTs require meticulous observation and accurate judgment in diagnosis.

2.3 Current status of diagnosis and treatment of LSTs

The diagnosis of LSTs, laterally spreading colorectal tumors, relies on a variety of technical means. The application of magnifying endoscopy and chromoendoscopy allows physicians to observe lesion characteristics more clearly for accurate diagnosis. Once diagnosed, treatment is usually based on endoscopic resection, such as endoscopic mucosal resection and endoscopic submucosal dissection, which are minimally invasive and recover quickly. With the advancement of medical

technology, the diagnosis and treatment of LSTs are increasingly accurate and efficient, bringing better treatment options and prognosis to patients [2].

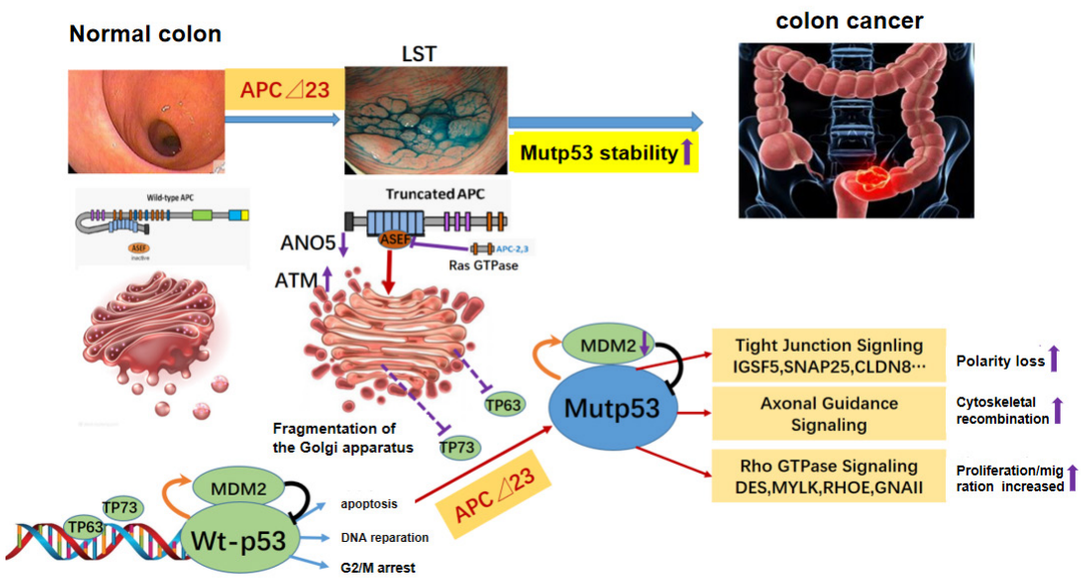

Figure 1. Schematic diagram of mechanism of APC truncation mutation regulating P53 promoting LST to CRC carcinogenesis

3. Screening and identification of molecular markers

3.1 Application of proteomics technology in tumor research

Proteomics technology is an important tool to study the expression pattern and functional pattern of all proteins in organisms from a holistic point of view and has a wide range of applications in tumor research. In cancer research, proteomics technology quickly and efficiently obtains proteomics data by measuring the quality and quantity information of proteins in samples. For example, in the study of breast cancer, scientists used proteomics technology to analyze the protein expression differences between breast cancer tissues and normal breast tissues and found a variety of proteins closely related to the occurrence and development of breast cancer, such as GCDFP-15 and AAG. The expression levels of these proteins in breast cancer tissues were significantly higher than those in normal tissues, which provided an important basis for the early diagnosis of breast cancer. In addition, proteomics can also be used for tumor classification, staging and prognosis. Through qualitative and quantitative analysis of proteins in tumor tissues, protein expression differences between different tumor types can be revealed, providing new ideas for tumor classification and treatment [3].

3.2 Application of iTRAQ quantitative proteomics technology in the study of LSTs

ITRAQ quantitative proteomics technology plays an important role in the study of colorectal laterally spreading tumors (LSTs). iTRAQ technology is a relative and absolute quantitative proteomics technique based on isotope labeling. It uses a variety of isotopic reagents to label the N-terminal and lysine side chain groups of protein peptides and achieves qualitative and quantitative analysis of proteins by tandem analysis with a high-precision mass spectrometer [4]. In the LSTs study, scientists used iTRAQ technology to analyze protein expression differences between LSTs tissues and normal colorectal tissues. Changes in relative abundance of proteins in different samples can be determined by comparing the signal intensities of labeled ions for specific peptides in different samples. For example, some proteins highly expressed in LSTs tissues, such as certain specific kinases and growth factor receptors, have significantly higher signal intensities than normal tissues. In addition, iTRAQ technology can also be used for molecular typing, staging, and prognosis of LSTs. Through in-depth qualitative and quantitative analysis of proteins in tumor tissues, the differences in protein expression profiles between different LSTs types can be revealed, providing new ideas for the precise treatment of LSTs. The application of iTRAQ technology in the study of LSTs has already achieved remarkable results, providing a powerful tool for revealing the pathogenesis of LSTs and finding new therapeutic targets [5].

3.3 Identification and analysis of proteins specifically expressed in LSTs

In the study of colorectal laterally spreading tumors (LSTs), the identification and analysis of specifically expressed

proteins is a key step to reveal their pathogenesis and find therapeutic targets. Scientists have successfully identified a number of proteins specifically expressed in LSTs through advanced proteomics technologies, such as iTRAQ quantitative proteomics. For example, LCN-2 (lipocalin-2) and MMP-9 (matrix metalloproteinase-9) were found to be significantly highly expressed in LSTs tissues. Compared with the normal control group, the mRNA and protein expression levels of LCN-2 and MMP-9 were significantly increased in the LSTs group, and this difference in expression levels was statistically significant Further analysis showed that the expression levels of LCN-2 and MMP-9 were positively correlated with the pathological grade of LSTs, suggesting that they may be involved in the malignant progression of LSTs. In addition, the concentrations of these two proteins in serum were also significantly higher than those in normal controls, providing potential biomarkers for the early diagnosis of LSTs. Although specific criterion values may vary according to experimental conditions, sample sources, and other factors, the above elaboration, proteins specifically expressed such as LCN-2 and MMP-9 play an important role in the pathogenesis and progression of LSTs and provide new targets and ideas for the diagnosis and treatment of LSTs [6].

3.4 Functional and pathway analysis of differentially expressed proteins

Functional and pathway analysis of differentially expressed proteins is an important link in biomedical research. For example, a differentially expressed protein called P53 is a tumor suppressor protein that responds to DNA damage and initiates apoptosis or cell cycle arrest. In pathway analysis, P53 is closely related to DNA damage repair pathway and apoptosis pathway, and its abnormal expression may lead to the occurrence and development of tumors. Another differentially expressed protein, named PTEN, is a phospholipase that inhibits the PI3K/Akt pathway, thereby regulating cell growth and survival. Loss or mutation of PTEN can lead to the development of a variety of tumors and is closely associated with aberrant activation of the PI3K/Akt pathway. Therefore, functional and pathway analysis of these differentially expressed proteins provides important clues to reveal the pathogenesis of the disease and to find therapeutic targets.

4. Study of critical molecular mechanisms

4.1 Relationship between gene mutations and carcinogenesis of LSTs

There is a close relationship between gene mutations and carcinogenesis of colorectal laterally spreading tumors (LSTs). Several specific genetic mutations play critical roles in carcinogenesis of LSTs. For example, mutations in APC (adenomatous polyposis gene) are one of the common molecular events in carcinogenesis of LSTs. The APC gene is located in the chromosome 5q21-22 region and is an important negative regulator of the Wnt signaling pathway. During carcinogenesis of LSTs, mutations in the APC gene may lead to aberrant activation of the Wnt signaling pathway, which in turn promotes proliferation and malignant transformation of tumor cells. Although there is no standard numerical analysis for specific gene mutations in LSTs carcinogenesis, studies have shown that the mutation frequency of genes such as APC is relatively high in LSTs carcinogenesis, suggesting that these gene mutations may be important biomarkers and therapeutic targets for LSTs carcinogenesis.

4.2 Signaling pathways and LSTs carcinogenesis

Signal transduction pathways are tightly linked to carcinogenesis in laterally spreading colorectal tumors (LSTs). Among them, several key signaling pathways play an important role in the carcinogenesis of LSTs, specifically: the Wnt/β-catenin pathway, and abnormal activation of this pathway can increase cell proliferation, promote epithelial-mesenchymal transition, and change the expression of transcription factors, thereby promoting the metastasis and invasion of LSTs cancer cells. The PI3K/Akt/mTOR pathway, by regulating cell proliferation, survival, and metabolic function, has an important impact on the development of LSTs. Abnormal activation of this pathway enhances the anti-apoptotic, proliferative, and metastatic abilities of cancer cells. Therefore, abnormal regulation and disruption of these signaling pathways may be key factors leading to carcinogenesis of LSTs.

4.3 Protein interaction networks and LSTs carcinogenesis

There is a complex relationship between protein interaction networks and carcinogenesis in colorectal laterally spreading tumors (LSTs). In the carcinogenesis of LSTs, the interaction network formed by some key proteins such as Akt1* and EGFR* plays a key role. Akt1 is located within the core subnetwork and has a high interaction with other genes and is involved in regulating the VEGF signaling pathway and promoting angiogenesis, development, and metastasis of tumors. Overexpression of EGFR, on the other hand, is also associated with carcinogenesis and a higher risk of metastasis in LSTs. Therefore, abnormalities through these protein interaction networks may lead to an imbalance in apoptosis and proliferation, which in turn drives the carcinogenesis process of LSTs

5. Conclusion

In summary, carcinogenesis of colorectal laterally spreading tumor (LST) is a complex multifactorial and multistep process involving multiple levels such as gene mutations, abnormal signal transduction pathways, and altered protein interaction networks. Through in-depth study of the molecular mechanism of LST carcinogenesis, it can not only better understand the pathogenesis of colorectal cancer, but also provide new ideas and methods for the early diagnosis, treatment and prognosis evaluation of LST. In the future, with the continuous development of bioinformatics, high-throughput sequencing and proteomics and other technologies, it is reasonable to believe that there will be a more comprehensive and in-depth understanding of the molecular mechanism of LST carcinogenesis, thus revolutionizing the prevention and treatment of colorectal cancer.

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