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Meta-analysis of the Expression Level and Significance of miR-21 in Cancer Tissues of Patients with Prostate Cancer

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Abstract: *Prostate cancer is the second leading cause of cancer-related death in men. MicroRNAs are thought to have a potential role in tumorigenesis. In this paper, the significance of the expression level of mir-21 in prostate cancer patients and its Meta-analysis were investigated. For this study, MiR-21 and prostate cancer detection methods were first described in detail, and then a model was established for the detection of prostate cancer, and the image was divided into foreground and background parts according to the selected threshold, and the prostate image was detected. The data of prostate cancer patients were collected, divided into four types: well-differentiated cancer, moderately differentiated cancer, poorly differentiated cancer and undifferentiated cancer, and then they were stained to analyse the changes in the expression level of miR-21 in the experimental subjects. The experiments showed that when circulating miR-21 levels were elevated, potential patients were 4.3 times more likely to develop cancer than healthy controls.*

Keywords: *Prostate Cancer; Cancer Tissue Cells; Mir-21; Expression Levels and Meta Analysis*

1. Introduction

Prostate cancer is a biologically heterogeneous disease with variable clinical outcomes. In some of these individuals, clinical progression is relatively slow and therefore does not require immediate treatment, or even treatment. Relative to this group, at least 75% of new cases have a potential risk of progression and require treatment. Prostate cancer is initially confined to the glands, then spreads into regional lymph nodes, and then hematogenously spreads to distant organs, especially bones. Because people's understanding of the mechanism of prostate cancer occurrence, development and metastasis is still very limited, it is impossible to distinguish the types of the disease with different malignant degrees, and CRPC and mCRPC cannot be effectively controlled. Since the introduction of prostate-specific antigen testing, most patients diagnosed with prostate cancer have been organ-confined. In some of these men, there is relatively slow clinical progression (indolent prostate cancer) and therefore do not require immediate treatment or even life-long intervention. The other group, at least 75% of new cases, has a potential risk of progression and requires aggressive treatment. How to distinguish these two types of patients is one of the hotspots of current debate and research. During prostate cancer treatment, prostate cancer progresses despite serum testosterone levels reaching castration levels. How to treat these patients with metastases or insensitive to antiandrogen therapy, radiotherapy and chemotherapy, there is no specific method. These currently intractable problems reflect the lack of understanding of the mechanism of the occurrence and development of prostate cancer.

At present, many scholars are studying the diagnosis and treatment of prostate cancer. Kim MY proposed that microRNA (miRNA) in urinary exosomes has become a biomarker of urinary system cancer due to its high stability. miRNAs have been implicated in many aspects of prostate cancer, especially biochemical recurrence and migration. But his research method is not applicable to prostate cancer [1]. Logozzi M said the prostate-specific antigen (PSA) test is the most common and clinically validated test used to diagnose prostate cancer (PCa). He utilized Nanoparticle Tracking Assay (NTA), an immunocapture-based ELISA and nanoscale flow cytometry. However, this method ignores the expression level of miR-21 in prostate cancer patients [2]. Stuopelyt K says the expression of various transcripts, including miRNAs, is markedly dysregulated in cancerous prostate tissue. The aim of his research is to determine the PCa-specific expression profile of miRNAs for subsequent use in

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non-invasive diagnostics. However, this method is still far from practical application [3].

An in-depth understanding of the role of the tumor microenvironment in accelerating tumor progression, understanding that prostate cancer is no longer considered a disease caused by abnormal proliferation of epithelial cells, but a prostate cancer epithelial cell and surrounding tissue interaction disease. The pathogenesis of malignant prostate cancer is not limited to cancerous epithelial cells, and the tumor microenvironment also plays a role. There are various signaling pathways between epithelial cells and interstitial cells. The extracellular interstitial components have been supporting the growth of tumor cells from the primary cancer site, to regional lymph nodes, and then to distant metastatic sites. Alterations in the tumor microenvironment are associated with the production of reactive stroma and influence events in tumor progression, such as proliferation, migration, and apoptosis. However, it is still unclear which mesenchymal cells regulate the epithelial cells and the mechanisms that cause the differences in the interstitial composition of prostate cancers of different pathological or histological origins. Therefore, it is important to identify the stromal components of prostate cancer and benign prostatic hyperplasia, and it is of great significance to assess the expression level of MiR-21 in prostate cancer through meta-analysis, data correlation and qualitative summary.

2. Overview of MiR-21 and Prostate Cancer Detection Methods

2.1 MiR-21 and Prostate Cancer

MiR-21 is ubiquitous in nature and one of the earlier miRNAs found in eukaryotic cells. Many studies have shown that inhibiting the expression of miR-21 not only inhibits the growth of MCF-7 cells, but also slows the growth rate of MCF-7 xenografts. Inhibition of the expression of miR-21 in glioblastoma cells led to the increase of apoptotic cells, indicating that it may regulate cell apoptosis by regulating apoptotic genes. Expression of miR-21 has been shown to be abnormal in various cell lines and cancer tissues. There is evidence that miR-21 is highly expressed in solid tumors such as liver cancer, lung cancer, and breast cancer, and is one of the most common highly expressed miRNAs. All these indicate that miR-21 participates in and regulates the occurrence and development of cancer, and it acts as an oncogene that promotes tumor growth in this process [4].

Histologically, the prostate consists of two parts: the stroma and the gland. Interrogation includes extracellular matrix, smooth muscle and fibroblasts. The glands are mainly composed of luminal and basal epithelial cells. In the continuous development of the treatment of prostate cancer technology, epithelial cells are the first to become cancerous and acquire malignant features. The interaction of cancerous epithelial cells with the surrounding stroma also plays a key role in tumor progression. The interaction between the epithelium and the interstitium leads to the formation of a reactive stroma. The reactive stroma regulates the proliferation, differentiation and migration of epithelial cells, and can also induce angiogenesis and epithelialization. Interrogation transformation, inflammatory response, drug sensitivity response and other biological activities. At the same time, the reactive stroma itself and its markers can provide information for people to distinguish tumor progression [5]. Research on the mechanisms and markers of prostate cancer epithelium-interaction interactions has attracted much attention.

2.2 Prostate Cancer Detection Methods

Prostate cancer (PCa) lacks specific clinical manifestations in the early stage. When symptoms appear, most patients have local invasion or distant metastasis and lose the opportunity for radical treatment. However, early PCa treatment has a positive effect, and most patients can be cured. Therefore, the early diagnosis of PCa is of great clinical significance. At present, the diagnosis of PCa mainly relies on the determination of serum prostate-specific antigen concentration, imaging examination, digital rectal examination and prostate biopsy under the guidance of transrectal ultrasonography.The flow chart of prostate examination is shown in Figure 1.

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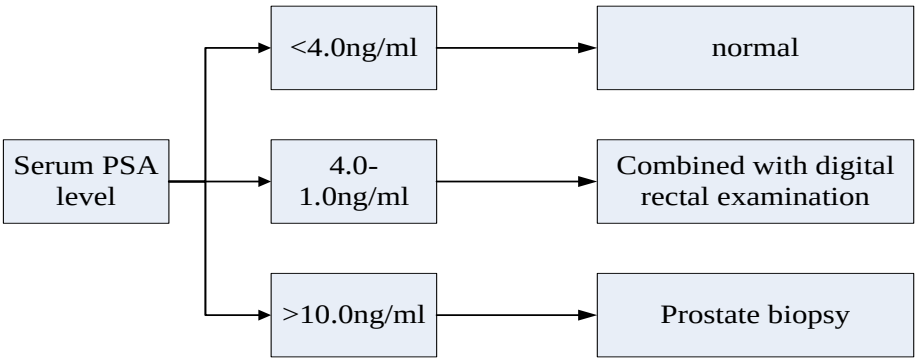

Figure 1: Prostate examination flowchart

2.3 Detection Models of Prostate Cancer

The image is divided into foreground and background parts according to the selected threshold. Pixels with intensities greater than the chosen threshold are called foreground, other areas are called background. Let the obtained main threshold T be the most suitable position for the firefly algorithm. Taking the existing energy curve pattern of T as the optimal position provided to the firefly algorithm, find the optimal threshold value closest to the image segmentation [6-7]. According to different quantitative and qualitative evaluation indicators, the optimal threshold is used to segment the input image, and the obtained results are analyzed. Therefore, regardless of the type or morphology of the input image, the method can obtain the optimal threshold to discover ROIs for efficient segmentation [8-9]. This automated decision-making will aid in the early detection of prostate cancer and can be integrated into healthcare solutions, sharing results on dashboards, and managing large volumes of data in clinical settings [10].

$$D = \frac{2\sum_{\mathrm{i}}^{N} \mathrm{p}_i g_i}{\sum_{\mathrm{i}}^{N} \mathrm{p}^2{}_i + \sum_{\mathrm{i}}^{N} \mathrm{g}^2{}_i} \quad (1)$$

In fact, the results observed experimentally are much better than those trained by the same network, which optimizes the polynomial logistic loss by reweighting the samples. Use this formula:

$$\frac{\partial D}{\partial \mathrm{p}_{\mathrm{i}}} = 2\left[\frac{g_i(\sum_i^N p_i^2 + \sum_i^N g_i^2) - 2p_j(\sum_i^N g_i p_j)}{(\sum_i^N p_i^2 + \sum_i^N g_i^2)^2}\right] \quad (2)$$

3. Design and Experiment of the Expression Level of MIR-21 in Cancer Tissues of Prostate Cancer Patients

This time, 6 normal prostate tissue samples and 50 cancer samples were collected first. The pathological diagnosis was made according to the Gleason scoring system, and the grading constant of cancer tissue: according to Gleason grading, Gleason score 2, 3, 4, and 5 were classified as well-differentiated adenocarcinoma, Gleason score 6, 7 were classified as moderately differentiated adenocarcinoma, Gleason score 8, 9 and 10 are divided into poorly differentiated adenocarcinoma and undifferentiated adenocarcinoma. The pathological diagnosis results were: 10 cases of well-differentiated prostate cancer, 24 cases of moderately differentiated prostate cancer, 10 cases of poorly differentiated and undifferentiated prostate cancer, and 6 cases of normal internal gland and external gland respectively. The first picture shows the intraprostatic glands: located near the urethra, consisting of small ducts and acinars, growing in the smooth muscle stroma around the urethra and branching into the anterior prostatic sphincter like a branch; the second picture is Extraprostatic glands: The ducts and acini are well developed. The ducts extend from the distal urethra to the posterior and lateral lobes of the prostate. On the coronal section, a cone-shaped area centered on the fumarole is formed. The bottom of the cone is the base of the prostate. ; The third picture is a well-differentiated prostate cancer tissue: the tumor is composed of simple small glands or simple large glands, but the difference is similar, the structure is uniform, and interstitial infiltration is seen; the tumor cells are larger in size and have darker nuclei , the tumor cells are mildly atypical, and the mitotic phase is rare;

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the fourth picture is a moderately differentiated prostate cancer tissue: under a low magnification microscope (×200 times), it can be seen that the tumor acinus is separated by the stroma, with different sizes and irregularities, composed of complex glands. , fused glands or cribriform glands; the fifth picture is a moderately differentiated prostate cancer tissue: under a high magnification microscope (×400 times), the tumor acinus can be seen in different sizes, shapes, and infiltration; tumor nuclei It is hypertrophic and hyperchromatic, with large and red nucleoli, and the cytoplasm is mostly alkaline stained; the sixth picture is a poorly differentiated prostate cancer tissue: the border is irregular, and the tumor is composed of scattered or lamellar cells, and the growth pattern is Sheet-like single cell type or acne-like carcinoma type, solid beam-like or sheet-like, few glandular ducts are formed, and the size varies greatly, and the structure is disordered; the tumor cells are small, with obvious atypia, and large nucleoli and mitoses are more common. , extensive infiltration, and changes in cytoplasmic staining. All specimens were histopathologically diagnosed, as shown in Figure 2.

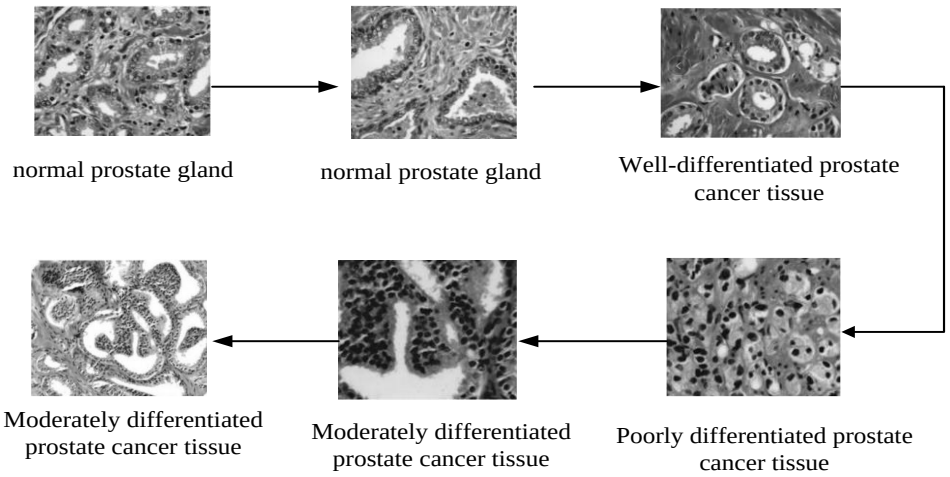

Figure 2: Pathological pictures of normal prostate tissue and cancer tissue stained by HE

4. Experimental Results

During the experiment, a total of 90 data samples were selected, of which 30 belonged to patients with benign lesions, 30 belonged to patients with prostate cancer, and the remaining 30 belonged to the healthy control group. The experimental results showed that in the collected data samples of prostate cancer patients and benign lesions, the expression level of miR-21 in patients was much higher than that in healthy people. The AUC value of serum miR-21 in distinguishing benign lesions from healthy controls was 0.670 (0.562-0.777). The AUC value of serum miR-21 in distinguishing prostate cancer patients from healthy controls was 0.831 (0.746-0.916). The AUC value of serum miR-21 in distinguishing prostate cancer patients from benign lesions was 0.710 (0.608-0.813). The cutoff value was 3.457, and the sensitivity and specificity were 64% and 76%, respectively. The details are shown in Table 1.

Table 1: Interruptible load characteristics

	AUC value	Sensitivity	specificity	cutoff value
prostate cancer patients	0.710	64%	76%	3.457
benign disease patients	0.670	56%	76%	1.502
healthy control group	0.831	70%	92%	2.937

MiR-21 is variable in prostate epithelial cells. When mixed probes were used for all samples, non-specific staining was observed. MiR-21 expression was analyzed by qRT-PCR using the same cell line. Increased miR-21 expression was found in PC3 cells with ISH-related results ($n = 6$, $p < 0.01$ compared to LNCaP cells). These data were all collected and we concluded that for GL-isolated miR-21 Additional studies may help assess patient outcomes. Figure 2 shows the staining of cancer cells for mir-21.

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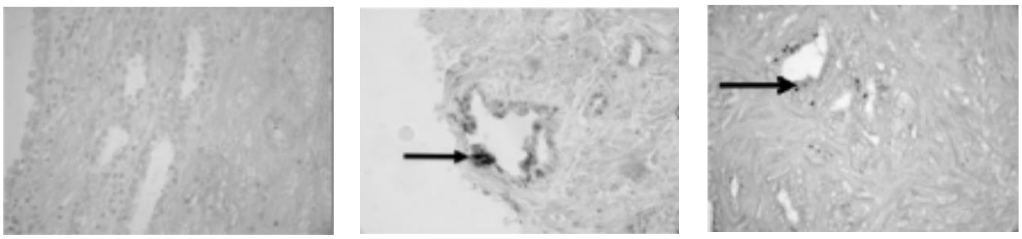

GL<7 **GL=7** **GL>7**

Figure 3: The staining of mir-21 in cancer cells

5. Conclusion

Among cancer cells, there are many different properties from ordinary cells, the most basic of which are infinite proliferation and abnormal differentiation. Exploring the genes and molecular mechanisms related to cell carcinogenesis and metastasis is still one of the important directions of oncology research. In this experiment, the miR-21 gene and its expressed protein were systematically studied, and it was confirmed that miR-21 is an oncogene and plays an important role in the occurrence, development and metastasis of prostate cancer. The combination of the expression level of miR-21 can help to identify the early diagnosis of prostate cancer, evaluate the invasiveness and prognosis of the tumor, lay a theoretical and experimental foundation for clinical application, and develop new and effective anti-tumor drugs for further research. Metastatic drugs provide new targets of action.

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