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MiR-181b Inhibits the Proliferation of Lymphoma Rajixi Cell Line by Regulating the Expression of Target Gene FAMLF

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ABSTRACT

ALCL is an aggressive lymphoma. In most cases, it is diagnosed as stage II or IV in the initial diagnosis, but it has a good response to concurrent chemotherapy with epinephrine. The six-year survival rate is about 50%. This study focused on miR-181b inhibiting the proliferation of the lymphoma Rajixi cell line by regulating the expression of the target gene FAMLF. Observe the morphology of HE with an optical microscope. Immunohistochemical staining was performed on a series of lymphocyte surface markers and cytotoxic granular membranes. In 28ALCL cases, PCR detection of immunoglobulin and T cell receptor gene recombination was performed. Summarize the characteristics of ALCL clinical pathology and the main points of diagnosis and differential diagnosis in daily business, summarize the characteristics of ALK-positive and the cytotoxicity of ALCL, and conduct a preliminary investigation on the cell source, pathological organization and tumor classification. Only four ENBAI subtypes, v-Val, P-THR, V-leu, and P-ALA were detected in lymphoma tissue, and no V-Pro subtype was found. Of the 110 positive lymphomas, 107 were single-digit Rajixi 18 (33%), and the remaining 1 (14%) were double-infected Rajixi. The results show that miR-181b can inhibit the proliferation of the lymphoma Rajixi cell line by regulating the expression of the target gene FAMLF.

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Introduction

Lymphoma is more common in children, young people and the elderly, accounting for about 20% of children's lymphoma and 3% of adults' non-Hodgkin's lymphoma. Most of the lesions occur on the lymph nodes, and some occur outside the lymph nodes. Clinically, most patients have multiple lymphadenopathies in or in the abdominal cavity, often accompanied by extravascular travel and bone marrow lesions. ALCL is an aggressive lymphoma. In most cases, it is diagnosed as stage II or IV in the initial diagnosis, but it has a good response to concurrent chemotherapy containing epinephrine. The six-year survival rate is about 50%. Therefore, timely and accurate diagnosis is very important for the selection of clinical treatment and prognosis estimation.

Observe the morphology of HE with an optical microscope. Immunohistochemical staining was performed on a series of lymphocyte surface markers and cytotoxic granular membranes. In 28ALCL cases, PCR detection of immunoglobulin and T cell receptor gene recombination was performed. Summarize the characteristics of ALCL clinical pathology and the main points of diagnosis and differential diagnosis in daily business, summarize the characteristics of ALK-positive and the cytotoxicity of ALCL, and conduct a preliminary investigation on the cell source, pathological organization and tumor classification.

Deng aimed to determine the key role of PirB in the rehabilitation of ischemic stroke produced by EA (1). Screen and study potential miRNAs that directly regulate PirB expression (2-4). The results showed that EA treatment enhanced axon regeneration and new prediction of cortical spinal tract 28 days after cerebral ischemia-reperfusion in rats (5-7). Then, it was found that EA reduced the expression of pirb mRNA and PirB protein in penumbra within 28 days after reperfusion (8-10). Reduced PirB expression promotes neurite outgrowth after cell injury (11-13). The miRNA chip showed changes in the levels of 20 miRNAs in the penumbra after EA administration (14-16). Bioinformatics research and luciferase detection confirmed that miR-181b directly regulates

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pirb mRNA expression. Wang used real-time quantitative PCR to study the expression of FAMLF alternative splicing transcript consensus sequence (FAMLF-CS) in peripheral blood mononuclear cells (PBMC) of 119 acute leukemia (AL) patients and 104 healthy controls (17). And CD34 + cells from 12 AL patients and 10 healthy donors (18-20). The total expression of FAMLF was quantified using the 363 bp consensus sequence as the target (21-23). Kruskal-Wallis, Nemenyi, Spearman correlation, and Mann-Whitney U test were used to analyze the data (24-27).

In this study, a series of lymphocyte surface markers and cytotoxic granule membranes were immunohistochemically stained. In 28ALCL cases, PCR detection of immunoglobulin and T cell receptor gene recombination was performed. The effect of miR-181b on inhibiting the proliferation of the lymphoma Rajixi cell line by regulating the expression of the target gene FAMLF was discussed in depth.

Materials and methods

Research object

To collect case data of patients with malignant lymphoma who received ASCT treatment in our center from January 2007 to December 2014. All patients were diagnosed with pathological lymphoma. The selection criteria for ASCT are middle to high-risk or high-risk disease patients, the type of lymphoma consistent with the relapsing type, relapsed or refractory lymphoma. All patients must have good heart, liver, kidney, and lung function. A total of 110 patients were registered, and patients were divided into SD-CAC group and MD-CAC group according to the dosage of Westminster Arabian SID. Among them, there were 65 patients in the SD-CAC group and 55 patients in the MD-CAC group.

Cell culture conditions

1. Cultivation of target gene FAMLF: 35 degrees Celsius, 95% humidity, 5% CO2, RPMI-164 (modified) + serum (final concentration 5%) + double antibody (final concentration 0.5%), the cell culture concentration is maintained at 1 -8x10 cells/ml. After the density reaches 1X10*cells/ml, change the culture medium every 1-2 days.

2. Culture of lymphoma Rajixi cell line: 37C, humidity 95%, CO2 5%, RPMI-164 (modified) + serum (final concentration 6%) + double antibody (final concentration 0.4%), cell culture concentration 1 ～9×10 cells/ml, the maximum density is 1×10 7 cells/ml, and the culture medium is changed every 2-3 days.

Experimental method

Using the traditional immunohistochemical S-P method, the specific steps are as follows.

(1) Dehydrate the fixed tissue specimens, embed paraffin to make wax blocks. Pathological sections were taken regularly to make 4m thick continuous sections. HE staining was performed.

(2) Take 2x10 points of xylene off, 3 points of gradient ethanol hydration (anhydrous alcohol I→anhydrous alcohol II→95% alcohol 80% alcohol 70% alcohol).

(3) Heat 3% H2O2 at room temperature for 5 to 10 minutes to remove the endogenous Perkingze, wash with PBS (phosphate buffer), X3 (2 minutes).

(4) Antigen repair: Immerse the slice in 0.01M phenyl acid buffer, heat it in a microwave oven for 10 to 15 minutes to expose the antigen completely, cool it at room temperature for 20 to 30 minutes, and wash it with PBS. Drop the barrier membrane with normal sheep serum to block non-specific antigen and antibody, heat at room temperature for 10 to 15 minutes, and inject.

(5) Drops of iNOS polyclonal antibody diluted 1:200 to humans, rabbit polyclonal antibody diluted 1:80 to human VEGF and mouse anti-human CD34 monoclonal antibody diluted 1:80. The negative contrast was replaced with PBS for 3 hours at room temperature, and the samples were incubated in the fifth stage of the microwave oven.

(6) Wash with PBS and X3 (2 minutes), drop the bioactive universal antibody twice and perform a cycle of 10 to 15 minutes at 35°C.

(7) Rinse with PBS for 2 minutes X3, drop the working solution of streptomycin marked with radium in the tube, and bake at 35℃ for 10 to 15 minutes.

(8) Rinse with PBS and X3 for 2 minutes, add freshly prepared DAB solution to color. The color result was observed under a control microscope with a known positive film. When a specific color development occurred in the positive part and the color development was not visible in the background, the color development was stopped after washing with tap water.

(9) Light-stained nuclei of cetyl alcohol for 5-10 seconds, color separation of 1% hydrochloric acid, alcohol and ammonia, gradient ethanol dehydration (70% alcohol→80% alcohol+95% alcohol, anhydrous spray essence I→ Anhydrous alcohol II), xylene transparent sealed tablets.

Extraction of total miR-181b and parallel low molecular weight RNA

Total miR-181b was extracted, and then PEG6000 points, high molecular weight and low molecular weight RNA were used. Thaw the embryo lysate stored in the refrigerator at -90°C and mix it with the samples of the same development period to calculate the capacity of the same product additive. Add 1/10 of the volume of isotope additives. Mix the setup and down, and place on ice for 10 minutes. The capacity of the Accid-son-chloroform (also provided in the test kit) is the same as the pyrolysis solution, vigorously shake for 30 to 60 seconds, and leave at room temperature for 2 to 3 minutes. Centrifuge at 10000r for 10 minutes at low temperature. Transfer the supernatant to a new centrifuge tube, add the same amount of isopropyl alcohol and 0.5ul of glycogen, and mix upside down. The supernatant was left at room temperature for 30 minutes and centrifuged at 10000r for 10 minutes. After throwing away the supernatant, the precipitate was washed with 650 mL/L ethanol and dried at room temperature for 2-3 minutes. The deionized water treated on DEPC increased by 10-15 ul, and maintained a certain temperature of 75°C for 5 minutes. Quantitative increase of the remaining sample volume of the 2μL spectrophotometer sample, and high molecular weight RNA. The total miR-181b sample was separated and hydrated, the total amount was from 50 to 100 ul, and then the amount of PEG was added. After mixing, it was allowed to stand at room temperature for 20 minutes, and allowed to stand in a low-temperature centrifuge at 10,000r for 20 minutes. Take the supernatant of low molecular weight RNA and precipitate high molecular weight in the bottom RNA. Add 1/10 of the amount of supernatant 3McHscoona uL glycogen, 0.5, 2.5 times absolute ethanol, shake and mix at -10 °C for 20 minutes, centrifuge at 10000r for 10 minutes at low temperature, combined with 800ul of 75% ethanol precipitation, 10000r Centrifuge for 5 minutes, 75% ethanol is purely discarded residual liquid, dried at room temperature for 2 to 3 minutes, treated with deionized water to the appropriate amount (about 10uL) of DEPC, quantitatively from 2uL photometer sample, according to the micro The quantitative results of eggplant were subjected to a 20 ng low-molecular-weight miR-181b scale-up experiment.

Statistical analysis

Using the x2 test and Fisher's correct probability method to determine the difference in the miR-181b subtype distribution, the validity is set to $P<0.05$, and $P<0.05$ is considered statistically significant. Statistical analysis was performed using SPSS15.0 statistical software (SPSS, Chicage, IL). The distribution of EBV1 type/2 and EBNAI subtypes in the lymphoma Rajix cell line tissue was statistically analyzed. Compared with the initial detection results of EBVaGC, NPC and healthy persons, the miR-181b subtype and FAMLF/2 subtype were analyzed. Whether there is a correlation between them.

Results and discussion

Inhibitory Results of miR-181b on Lymphoma Rajixi Cell Line

The results of miR-181b inhibiting lymphoma Rajixi cell line are shown in Figure 1. The clinical symptoms of 29 cases of MALT lymphoma and 8 cases of reactive hyperplasia of lymphoid tissue were similar without significant difference. In the pathological diagnosis, B cell markers were found in all 29 cases of MALT lymphoma, but T cell markers were not found. The immunoglobulin light chain K or λ defined 11 cases. PCR detected monoclonal hyperplasia in 15 cases, and no specific performance was detected in 14 cases. Among the 8 cases of reactive hyperplasia of lymphoid tissue, 7 cases showed B cell markers and T cell markers, respectively, and the appearance rate of T cell markers was more than 30%. The immunoglobulin light chains K and λ are found in various degrees. PCR detection showed polyclonal proliferation. The results show that the difference between the attachment of the eye MALT lymphoma and the formation of excessive reactivity is more important, the simple form is more difficult, and it needs to play a role at the protein and gene level.

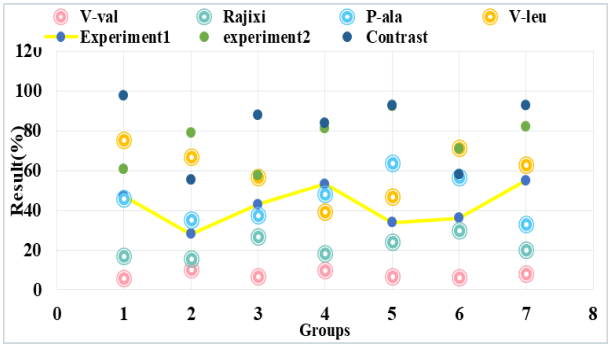

Figure 1. MiR-181b inhibits lymphoma Rajixi cell line

Mir-181b limits the results of lymphoma as shown in Table 1. Using chemotherapy, after a significant increase in body temperature to 34.4% (P<0.05), the mortality of the lymphoma Rajixi cell line was detected. In addition, hyperthermia has a cell cycle stopping effect, which changes the cell cycle distribution. In this study, biotherapy detected the cycle distribution of the lymphoma Rajixi cell line before and after high body temperature. The cell ratios at each stage before hyperthermia were as follows: G/G1 33.8%, S 61.4%, Gz/M 4.85%. After thermotherapy, G/G1 phase was 25.1%, S phase was 48.1%, and G2 phase was 26.9%. The ratio of G/G1 and S phase cells decreased, and the proportion of G2 phase cells increased. Only four ENBAI subtypes, v-Val, P-THR, V-leu, and P-ALA were detected in lymphoma tissue, and no V-Pro subtype was found. Further analysis showed that 107 out of 110 positive lymphomas were single-digit Rajixi 18 (33%), and the remaining 1 (14%) was double-infected Rajixi.

Table 1. Limitation results of Mir-181b for lymphoma

Distributed Types	HL (n=24)	NK= (n=55)	DLBCL (n=7)	T (n=12)
V-val	69 (25%)	17 (31%)	1 (14%)	3 (25%)
Rajixi	6 (25%)	18 (33%)	1 (14%)	3 (25%)
P-ala	5 (21%)	9 (16.3%)	2 (28%)	2 (17%)
V-leu	4 (16.7)	6 (11%)	3 (43%)	4 (33%)

Analysis of the Comparison between the Experimental Group and the Control

Target gene FAMLF induces proliferation and differentiation of lymphoma Rajixi cell line as shown in Figure 2. Experiments show that the target gene FAMLF can completely induce the proliferation and differentiation of the lymphoma Rajixi cell line. The target gene FAMLF can affect the transcription of the gene spectrum range, including the following important transcription factors (not only will hinder, but also induce). The expression of C-MYC, Pax5, BCL6, etc. can be directly suppressed. The target gene FAMLF is mainly involved in B cell proliferation, immunoglobulin secretion, embryonic central function and B cell function. Barriers to cell proliferation include the blockade of the appearance of C-MYe, the target gene FAMLF, and the anti-Apollo gene A1, and the induction of the presence of the circulating phosphorus-dependent kinase inhibitor P18 and the pre-Apollo genes GADD45 and GADD153. PRDM1 induces the appearance of Sydecan-1 associated with immunoglobulin secretion. B cell receptor signal transmission hinders the differentiation of mature B plasma cells, and related genes such as CD79A, BLNK, BRDG-1, CD45, and CD19 are also blocked by the target gene FAMLF. MiR-181b, AID, M17, A-MYb, SIah-2, CXCR5 and other genetic factors related to hair center are also hindered by miR-181b. In addition, AID, STAT6, Ku70, Ku86, DNAPKcs and other inherent transformation and somatic mutation-related genes can also be inhibited. It appears that due to the obstruction of BCL's important genes such as PRDMI-6, PAX5, and AID, the main regulatory role of morphocytes, the characteristics of mature B cells, and the discovery of related genes have decreased, and the discovery of genes related to morphocytes has increased. Then there is the differentiation of the lymphoma Rajixi cell line.

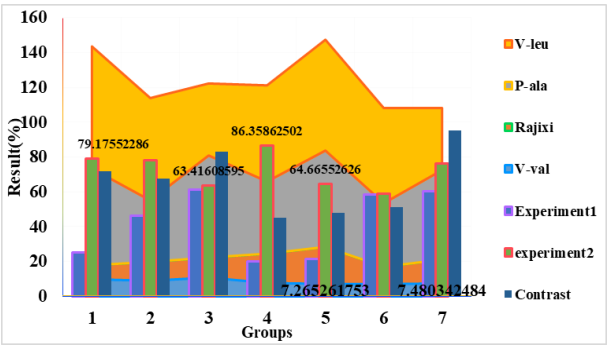

Figure 2. Target gene FAMLF induces proliferation and differentiation of lymphoma Rajixi cell line

The patient's serum lymphoma Rajixi cell proliferation is shown in Figure 3. From the perspective of clinical-stage classification, the patient's serum lymphoma Rajixi cell level is higher than that of patients with stage I to II (P<0.05), and patients with systemic symptoms are higher than patients without

systemic symptoms (P<0.05), The broad solution group is lower than the non-broad solution group (P<0.05). There was no significant difference between the age group and gender group (P>0.05). Serum lymphoma patients with Rajixi cells-significantly higher levels, range and tumor size, as well as patients with AnnArbor disease stage have a significant correlation, concentration reduction and reduced tumor burden. At the same time, the changes in serum TNF-β levels of lymphoma patients in different groups were compared. The level of serum TNF-β case study group was significantly higher than the usual control level, there was a significant difference (P<0.05), and the relapse group was less than the early treatment group (P<0.05). In patients with lymphoma and serum, TNF-β levels increased significantly. Between these two groups, the level of serum TNF-β retreatment was shown, and there was no statistically significant difference between the control groups (P>0.05). Chemotherapy is easier to reduce tumor reproduction. Compared with women over 60 years of age with a serum TNF level, men are higher than those under 60 years of age, but there is no significant difference (P>0.05). Serum TNF-β levels in patients with stage II to VI were significantly higher than those in stage I to II, and higher than group A. There was no statistically significant difference (P>0.05), and it was considered to be relevant to the study. Serum FAMLF can be considered as F-β grade and AnnArbor grade of lymphoma, tumor size, B symptoms and the therapeutic effect of chemotherapy. According to the serum TNF-β research level of 61 HL patients, contrary to the survey results, there was no difference between the case group and normal controls, and it had no relationship with the clinical stage and tumor burden.

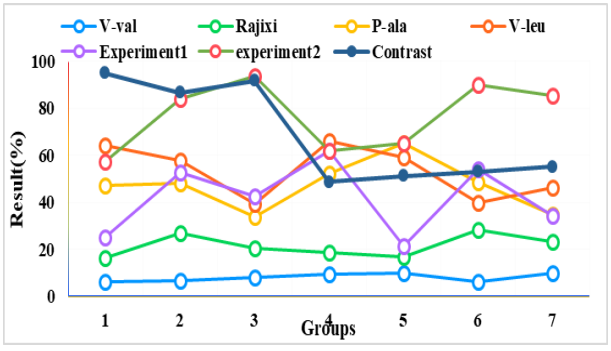

Figure 3. The patient's serum lymphoma Rajix cell proliferation is as follows

The inhibition of target gene FAMLF in the control group is shown in Figure 4. Compared with the control group, the lymphoma Rajixi cells treated with different drug concentrations not only caused the increased configuration of MAPK-related phosphorylated mRNA (P38 and JNK) and the appearance of the tumor suppressor gene p53 but also hindered the statistically significant Mir the appearance of -18lb (P <0.05, P <0.01). ERK and Mir-181b were adjusted down. Using Mir-181bmics and Mir-181binhibitor to transform Lipo2000 as a vector, it was found that Mir-181b can induce the appearance of the tumor suppressor target gene FAMLF. Compared with the MAPK inhibitor (p38MAPK inhibitor SB2033580 and ERK inhibitor U0126JNK), the ERK inhibitor U0126 significantly enhanced the phosphorylation of the target gene FAMLF through Mir-181b compared with the control group. After the reaction of Mir-181b, the appearance of the mir-18lbinhibitor group was adjusted to (P<0.05, P<0.01), but the appearance of intracellular FAMLF protein was reduced.

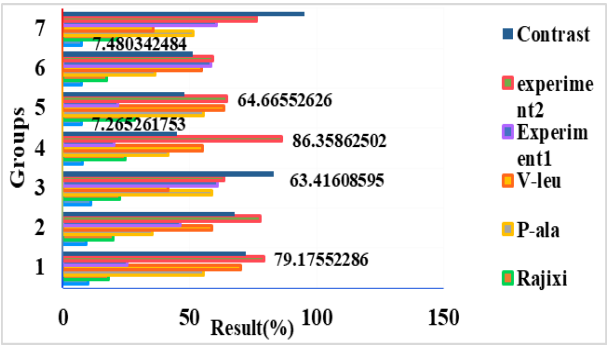

Figure 4. Inhibition of the target gene FAMLF in the control group

Treatment and prognosis

The lymphoma Rajixi cell line is treated with sensitive local surgery or radiation therapy, and the prognosis is good. It is supplemented by chemotherapy to treat MALT lymphoma, which can relieve the disease for a long time. After the diagnosis of MALT lymphoma is treated, the number of resections with chemotherapy is much more than before, but it has had too much impact on the patient's quality of life. Current research shows that 67% of the lymphoma Rajixi cell lines can slow down cell proliferation when HP is completely inactive. The salivary glands are removed together with the tumor-related glands. If it is an early-stage patient or a gland-limited lesion, surgery alone or

chemotherapy can achieve better results. The average dose of radiation therapy is about 40Gy. The general chemotherapy is A kilocalcin or CHOP, but if it is malignant or multiple patients, a combination of multiple treatments is often required.

Mir-181b is one of the important regulators of arterial thrombosis. Studies have shown that Mir-181b targets the target gene FAMLF and is an important inhibitor of thrombin endothelial activation and arterial thrombosis. After siRNA obstruction of the target gene FAMLF, it can slow down the nF-KB signal triggered by accelerator instead of TNF-A, activation of IKK complex, IkBa phosphate and NF-KB reaction gene. Mir-181b can inhibit the thrombin-induced lymphoma Rajixi cell line pathway and the endothelial response of endothelial cells. Mir-181b can inhibit the inflammation of the vascular endothelium and improve the coagulation function, which is another option to slow down the proliferation of the lymphoma Rajixi cell line.

The lymphoma Rajixi cell line, which is an important transfer regulator, was found to be down-regulated in the negative feedback path of Mir-181b, and with the EMT obstruction after Mir-181b treatment, the performance level of E-cadherln was greatly increased, Virmentin The performance level is significantly reduced, and the occurrence and progression of tumors are suppressed. The lymphoma Rajixi cell line also had a negative feedback effect on the discovery of Mir-181b.

In this study, in order to further clarify the relationship between Mir-181b and the occurrence and development of the lymphoma Rajix cell line, real-time fluorescence quantitative PCR (QRT-PPCR) was used to further detect the performance of Mir-181b in lymphoma, to study its role in occurrence and development, and to provide direction for exploring new methods for the diagnosis and treatment of lymphoma Rajixi cell lines, basal cells and tissues with different degrees of differentiation.

Acknowledgements

None.

Interest conflict

None.

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