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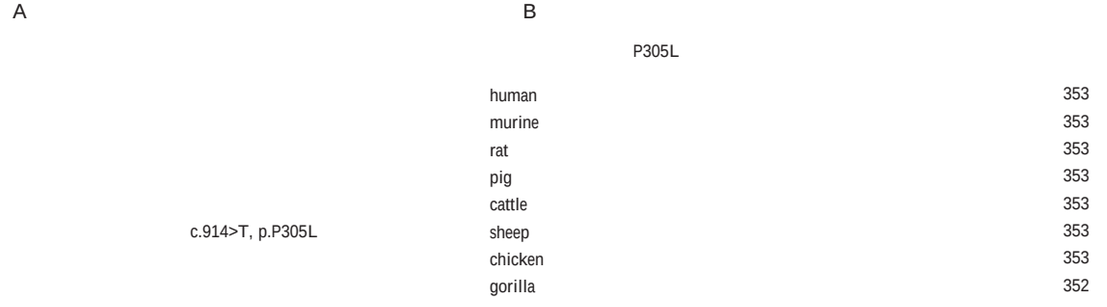

A. Sanger KIF1A c.914C>T p.P305L
B. KIF1A p.P305L KIF1A 294 353
Sanger KIF1A p.P305L

Figure . . . Sanger sequencing results of proband family and KIF1A gene p.P305L amino acid sequence of different species

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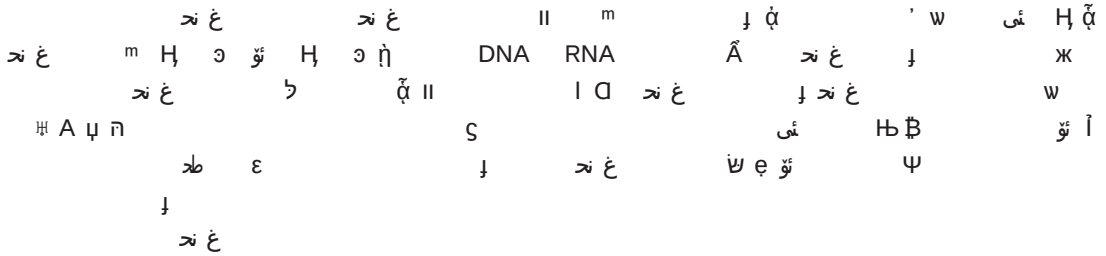
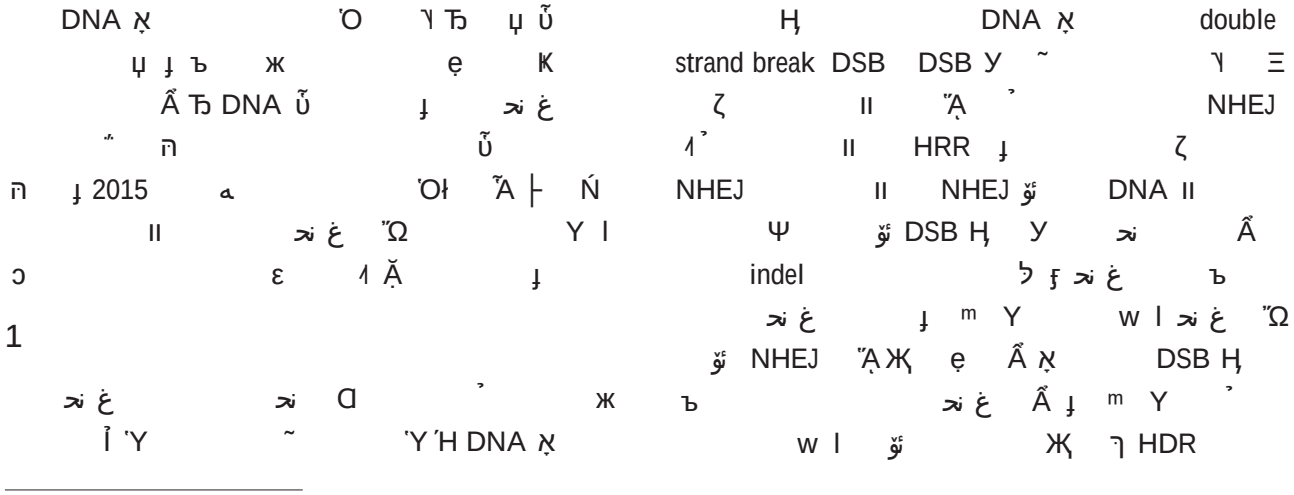


HUA Liang ZHU Bing
Central Laboratory of Guangzhou Women and Children s Medical Center Guangzhou Guangdong China 510120

ABSTRACT Gene editing refers to a new technology for site specific modification of the genome. Using this technology you can accurately locate a certain site in the genome cut the target DNA or RNA fragment at this site and insert a new gene fragment. This process simulates the natural mutation of genes by artificial means and then achieves the purpose of modifying and editing the original genome of the organism. Since its birth gene editing technology has experienced five generations of development the technology has become more and more mature and the editing accuracy has also been improved. It has been more and more widely used in various biological fields including disease treatment and has become a research hotspot in recent years. This article briefly reviews the progress of researches on gene editing technology and the therapeutic applications.

KEY WORDS Gene editing Therapeutic application



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2.2 Zinc finger protein ZFP
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DNA ė ɟ ZFN ζ Ƀ Нь ậ ү ´
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ę Ъm ǐ ɟ

2.3 ė Transcription activator like effector nucleases TALEN
Ά ZFN Ч TALEN Ş Ξ ŏ m
ŏ 33 35 Y ےز Ͳ ẃ Ң Нь
12 Ң ү 13 Ң Ξ Y ' Ь ےز ےز ậ ´
DNA ''Ω ę Ωm ~ ''Ạ N 5′T
w ɔ ' w ‴ً Ң Нь 12
Ң ү 13 Ң Ξ Y ' Ь ےز ےز ặ ~ ''Н ω Ỽ
ă DNA ''Ω ɟ Ð m ŏ Ά ZFN ً
''Ạ Ǐ 'Y Fok I ɟ TALEN ğ m ɔ
ẋ Ъ ZFN ğ Ͳ
ү ɟ ѿ ğ ж ' ү I
Ψ NHEJ ү HDR ɟ ж TALEN
I ZFN ғ З К Ƀ Ј
ъ ''Ạ Ъ ę Нь ےز ė ɟ

2.4 ع ''Ω/
ع ''Ω Ă clustered regularly in terspaced short palindromic repeats/CRISPR associat ed proteins CRISPR/Cas
CRISPR/Cas9 sgRNA Ά DNA
Ψ ך PAM ''Ω ɔ ےز ė Ў Ő
Cas9 U‘tP ےP ė0 'Y ´H

2.6 غ ﻨﺤ ⅃
Ҟ װ ⅃ ˘
ぇ ˊ ᾅ ↄ ﻲ dCas9 ↄ ᾳ
dCas9 ˜ ᾳ ˊ DNA ﯙ
Ң ↄ ﻨﺤ غ ɟ З ぇ
dCas9 ˊ Ђ CRISPR ﯙ ⅃
غ ﻨﺤ م ΄Y dCas9 ﻨﺤ غ
Ẻ ẫ ⅃
ɛ Ι Ỉ ﻨﺤ غ װ ⅃ Ђ ﻨﺤ ɟ

З

ﻨﺤ غ ж ﯙ Ι Ỉ ⅃ Ι ˥
Ђ ʽ ɟ Ι Ỉ ﻨﺤ غ ₿ ˜
ﻨﺤ غ Ι
˜ Ι З װ ʼ Њ
Ə Ḣ ɟ

3.1 Ι ﻨﺤ غ
Ι ﻨﺤ غ ъ ж ↄ ˥
ﯙ ﻨﺤ غ ˜ ع Ң w
ᾅ ɟ
Ђ ﯙ Њ Ђ Ά φ ẍ
ɟ ﻨﺤ غ ᾅ ˜
ↄ Ђ ⅃ ẍ
╥ ﻨﺤ غ ɟ X O ˊ ẍ ɞ
ɞO ˊ ẍ ɞ ↄ
Ẽ ˆ ɞ Ẽ ˆ ɞWiskott Aldrich
ˊ ⅃ ﺌﻰΨ [4,5] ɟ
ﻨﺤ غ ⅃ NHEJ ﻨﺤ غ Ẩ
Ə Њ ₿ ⅃ ﺌﻰ
Ψ ﯙ Ỉ [6] ɟ ʄ HRR ﻨﺤ
غ ς Ό Ὼ ɟ ﯙ ῗ
Ҟ Ψ ה Ђ ₿ Ι
ï [7] ﺌﻰΨ [8] [9] ⅃ X
IgM ˊ [10] ɟ

3.2 Ι Ỉ ﻨﺤ غ
ↄ ῗ ъ ↄ
Ι Ə˜ ﺌﻰ ع Ι Ỉ
Ὼ Ι Ỉ ﻨﺤ غ ɟ
Ẽ ˆ Duchenne muscular dystrophy DMD ﻨﺤ غ ኃ ⅃
ኃ ɟ ᾳ AAV Ι Cas9 ⅃ sgRNAs
ᾅ DMD Ι Ỉ ʄ DMD ﻨﺤ غ
Ő NHEJ ﻨﺤ غ װ
ъ ǖ ʄ ⅃ ↄ ⅃
ʽ ↄ [11,12] ɟ
ᾳ AAV Ι ˊ NHEJ ﻨﺤ غ
ЊΨ Ҟ ɟ Ꜻ
ǖ ᾅ Ψ З
ɟ Φ [13] Ι Ҟ
ኃ [14] w ẘ ç Ẉ 10 [15] ɟ
Њ ﻨﺤ غ ﻨﺤ غ ӌ
ẹ ʄ Ι Ỉ Ι Ỉ HRR ɟ
Њ ᵐ З ӌ
ï [16] ɞφ ﻲ Ꭿ [17] ɞ ɞ
ɞ ⅃ [18,19] ɟ Ꜻ
ᵐ ӌ Ψ ﻨﺤ غ ﻲ
ኃ ɛ ﻲ [20] ɟ

3.3 ﻨﺤ غ
ﻨﺤ غ Њ ɟ ж ˧
gRNA ⅃ AAVs Cas9 ʽ˘ Ђ
HIV ﻨﺤ غ Ψ LTR ⅃ gag ┘ DNA ﻨﺤ
غ [21] ɟᵐ ⅃ ኃ ╥
˜ HIV ﻨﺤ غ Ξ Y ┘ Ξ Y gRNA
ʼ w ẫ Ặ [22] ɟ
φ ﻲ Ẻ Ẫ ɵ ˊ DNA cccDNA
ẹ ﯙ Ψ Њ Ѣ ΄Y cccDNA ẅ
⅃ Ő غ
ʽ ɟ ж ˧ HBV ˜
gRNA ᾳ Cas9 ΄Y ΄H cccDNA Y
⅃ ኃ ˜ ζ NHEJ Ặ ẹ Ђ װ
ɟ ʼ w HBV Ё Ắ ʁ [23] ɟ

3.4 Ҟ ﻨﺤ غ
Ҟ װ Ά ж Ặ
ﻨﺤ غ ɛ Ҟ Ặ
⅃ à Ђᵐ ẫ ɟ ﯙ
Ψ Ҟ ʼ w ﻨﺤ غ ﯙ Y
H ǖ Ψ ẫ Ё ɟ ˜ ⅃
DNA ﻨﺤ ˊ ﯙ Ң
ﻨﺤ غ Ặ [24] ɟ ﻨﺤ Њ ẃ Ђ ↄ
CRISPR ﯙ Y ζ Ѷ ẃ ﺠ
Ẽ ↄ ﺿﻢ ↄ ⅃ ʼ ﻨﺤ غ w
ẘ ﻨﺤ غ [25] ɟ Cas9 ﯙ Ι Ỉ
ʼ w Ꭿ Ҟ ﺸ Ỉ ﻨﺤ غ [26]
Њ Ẽ ˆ ⅃
ﻲΨ ɟ CRISPR Cas9 Њ Ι Ỉ
ኃ ﻲΨ ʄ Nrl ẉ

ↄ ڑ ζ ڜ ڠ ẉ
ε ۪ CRISPR Cas9 ’
Ά̈ Ὼ P [27] ɟ

4

ﷺ ˘ ‖ Ψ ڜ ڠ ך Ъ
ɟ ά 2013 ~ CRISPR/Cas9
ה Ⱨ ך Ъ ɟ [A] 3 Ė
Ⱨ Ъ[m] ã̃ ш
ώ̈ ï ɟ ڜ ڠ
Ⱨь ├ ⱶ ƛ 3
ⱶ ɟ ώ̈ [m] ш د ɟ Ж̌
Ⱨ м [m] ƛ ẇ ʄ
ↄ ɟ 3 Ж̨ ᾰ [m] د ﷺ
[m] ’ Ж̨ ε ζ ɟ

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B27

ж Ɑ B27 ɑ ƚ ɨ ɟ HLA B27
ɻ ɻ EB ɔ ɲƶ Ɛ̃ ɔ ɟ ɾ ɲƶ ɕ DNA Ɣ̈Ạ
ɑ ƚ ɨ ɟ 4 ╟ Ə ╥ Ң HLA B27 Ң̇ ɯ
PCR ɢPCR SSP ɢSBT ɑ ƚ ɨ e ɑ ƚ ɨ ǯ -20 ɻ 25
φ ɤ ǎ 3 ɻ ᶍ ₱ ɟ ' Ɣ̈Ạ HLA B27 ɑ ƚ ɨ ₿˘ 3 ʀ
HLA B27 DNA ɻ 7 ʀ HLA B27 DNA ɟ ɯ PCR ɢPCR SSP ɢSBT
╟ Ə ƚ ɨ e Ɣ̈Ạ ɟ ƚ ɨ ᶍ ₱ m ƚ ɨ 3 ˜ ɯ ɟ ж
Ɑ B27 ɑ ƚ ɨ ˘ ᶍ ´ ' Ҥ ж Ɑ B27
Ң̇ ɵ ɟ
ж Ɑ B27 SBT ɑ ƚ ɨ ╟ Ə

HU Zebin GAO Fei SUN Nan SUN Binyu LI Lili SUN Jing QU Shoufang HUANG Jie
Division of In Vitro Diagnostic Reagents National Institute for Food and Drug Control Beijing China 100050

ABSTRACT Objective To establish a national reference material for HLA B27 nucleic acid detection. Methods Fresh peripheral blood of HLA B27 positive and negative volunteers was collected transformed with EB virus and cultured to establish immortalized cell lines. The genomic DNA was extracted from the cells and prepared for the national reference material which was verified by the next generation sequencing technology. Moreover the accuracy of the national reference was verified by fluorescence PCR PCR SSP method and SBT sequencing method with HLA B27 nucleic acid detection reagents from four collaborative manufacturers. The stability after 3 cycles of freezing and thawing at - 20 and 25 and homogeneity of the national reference materials were studied as well. Results The national reference materials of HLA B27 were successfully prepared including 3 HLA B27 positive DNA samples and 7 HLA B27 negative DNA samples. The reference materials were accurately valued by SBT sequencing and other methods and the homogeneity of reference material was consistent. The reference material is stable after 3 cycles of freezing thawing which met the requirements of the national reference material. Conclusion All indexes of the national reference material for human leukocyte antigen B27 nucleic acid detection meet the requirements and can be used for the performance evaluation of human leukocyte antigen B27 nucleic acid detection kit.

KEY WORDS Human leukocyte antigen B27 SBT sequencing National reference materials Collaborative calibration

ж Ɑ human leukocyte antigen HLA B27 Ɑ Ά Ặ 90% ę HLA B27 Ɑ ε ж Ψ c 5%~10% ε [1 3] ɟ ц 70 HLA B27 Ж ىي ה ۱ ğĭ Ψ ه ж Ψ B2705 ۱ B2704 Ж ىي ŏ ΄Y Ά ΄Y Ặ [4 6] ɟ نح غ ה ۱ Ặ ΄Ị ה ɔ نح Ⱨь ´ א polymerase chain reaction PCR HLA B27 ε í ɔ [7 9] ɟ ѽ ه HLA B27 ΄Ị ه ל ɬ ΄Ị [m] Ţ ɟ ε ٦ HLA B27 í ’ ε í w ΄Ω Ψ ه ɬ ɬ l ΄Ị Ⱪ ΄Ị ѽ ΄Ậm HLA B27 ɵ ه ל ɬ ɟ

1

1.1

1.1.1 ζ ΄Ị

ж ۱ ŏ ɵ A ۱ J نح Ж ←Ш ặ w نح غ DNA ٦ ΄Ị HLA ŏ نح غ ŏ ىي ΄Ị Qubit ssDNA Assay Kit Invitrogen MGISEQ 2000RS ΄Ị ڇ ╞ ặ w ж Ɑ B Ⱨ نح غ ŏ ŏ ىي ΄Ị ←Ш ╪ ė ặ w ж Ɑ B27 ΄Ị ψ PCR ü oy ặ w SeCore HLA B Ⱨ ŏ ىي ΄Ị ←Ш ΄A ├ ặ w ж Ɑ B*27 نح غ ŏ ىي ΄Ị SSP ۱ ψ PCR ĸ ặ w ɟ

1.1.2 ζ Ⱥ ƀ

MGISEQ 2000RS Ⱥ ڇ ╞ ặ w نح غ ⱨ Ⱥ S1000 Bio Rad ɕ نح غ ŏ Ⱥ 3730xL ThermoFisher ←Ш ╪ ė ặ w SLAN 96P ã ├ PCR ŏ ü oy ặ w ABI 3130/3130XL DNA Ⱥ/ نح غ ŏ Ⱥ ←Ш ΄A ├ ặ w ABI GeneAmp PCR System 9700 ɕABIReal Time PCR Systems 7500 ĸ ặ w ɟ

1.2

1.2.1

[n] ל Ά ۱ Ъ ̓ Ш ɟ 2018 2 2019 2 Ă ặ HLA B2704 2 ϛ ɕHLA B2705 3 ϛ ɕHLA B27 8 ϛ ɟ 10 mL ۱ Ậm /

΄H Ψ 2~8 ٦ ɟ Ậ ΄Ạ ã ɔ ɔ Ά نح Ế ɕă ɟ ~ نح Ế ɟ

1.2.2 ه ל ɬ ΄Ạ Ά

۱ ɔ [10 11] نح غ DNA ٦ ΄Ị Ə ٦ 10 ϛ ˈ نح غ DNA ƒ Ⱨ NanoDorp ę OD260/OD280 [e] ġ ΄H DNA ɟ ƒ Qubit Fluorometer3.0 10 ϛ DNA ~ 20 ng/ L next generation sequencing NGS Y ɟ ´ DNA ŏ ɔ ɟ

1.2.3 ه ל ɬ ╟Ə

ŏ ặ ƒ 4 ╟Ə ╥ Ⱨ HLA B27 ΄Ị ه ל ɬ ╟Ə ΄Ị Ш Ə ɟ Y 1 PCR Y 3 ɟ Ш ל ɬ φ~ Ő ɟ

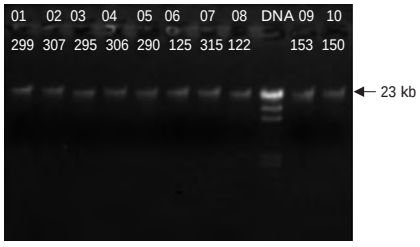
1.2.4 ه ל ɬ ۱ ڇ ₱

٦ A ه ל ɬ ğĭ -20 Ά 25 φ א ă 3 1 [m] φ~ ŏ ặ ƒ ɕPCR ɕSSP HLA B27 ΄Ị ל ɬ ɟ Ɠ ٦ ΄O ɕ ه ל ɬ ƒ HLA B27 ΄Ị ל ɬ ڇ ₱ ɟ

2

2.1 ه ל ɬ ΄Ạ Ш

HLA B27 ه ל ɬ Ƀ 10 ϛ نح غ DNA 3 ϛ HLA B2705 ɕ7 ϛ HLA B27 ɟ ΄H 01 10 ˝ DNA ặ ΄Y ŏ ğĭ 23 kb ˆ ћ 1 ɟ



DNA ε DNA Hind digest marker 01 10 ŏ ̈ ε 10 ϗ ɲ ɛ DNA J Y ˝ 3 Ӈ ˀ 1 Ψ ˝ /ώ 3 Ӈ ɟ

1 10 DNA

Figure 1 The quality of extracted genomic DNA from 10 Samples

01 10 ˝ OD260/OD280 e ϫ ğ 1.80~2.15 φ DNA ´ NGS Y HLA B Ӈ 4 Ӈ ŏ ɲ ğ ŏ ی HLA B Ӈ ŏ ی ϫ Ά φ ώ ۷ ɲ ğ DNA ŏ ی ɱ m ~ 30 L l ŏ 1 ɟ 2.2 ۸ ל ɨ ╟ Ə 4 ╟ Ə ╥ Ӈ ŏ ̈ A ɶ B ɷ C ɶ D ɥ PCR ɲ ğ ŏ ی sequence based genotyping SBT ɷ ẉ PCR ɷ۷ PCR ΄Ω sequence specific primer SSP ۸ ל ɨ Ъ 2 ɟ

2.3 ۸ ל ɨ ۷ ϫ ₱

ƒ A ╥ Ӈ HLA B Ӈ ɲ ğ ŏ ŏ ی ̓Ӈ SBT 3 ל ɨ ۷ 2 א ă 3 ~ ל ɨ ƒ C ╥ Ӈ ۷ D ╥ Ӈ HLA B27 ̓Ӈ PCR ۷ SSP 3 א ă 3 ~ ל ɨ ɟ 3 ɟ

1 10 DNA

Table 1 Verification results of genomic DNA from 10 Samples

˝	ŏ	ng/ L	ŏ	l	L	A260/A280	HLA B ɲ ğ ŏ ی	ל ɨ ŏ
CNGB030299/HLA19061 01	20		30			1.94	B*15:27 B*38:02	
CNGB030307/HLA19069 02	20		30			1.82	B*13:01 B*35:03	
CNGB030295/HLA19057 03	20		30			1.89	B*15:11 B*51:01	
NGB030306/HLA19068 04	2		30			1.89	B*08:01 B*40:06	
CNGB030290/HLA19052 05	20		30			1.84	B*52:01 B*58:01	
CNGB030125/HLA18005 06	20		30			1.88	B*13:02 B*15:02	
CNGB030315/HLA19077 07	20		30			1.88	B*13:01 B*58:01	
CNGB030122/HLA18002 08	20		30			1.83	B*27:05 B*48:01	
CNGB030153/HLA18024 09	20		30			1.89	B*27:05 B*44:03	
CNGB030150/HLA18021 10	20		30			1.8	B*27:05 B*58:01	

2 4

Table 2 Verification results of references by detection kits from 4 manufacturers

˝	A ╥ Ӈ SBT	B ╥ Ӈ SBT	C ╥ Ӈ PCR	D ╥ Ӈ PCR	D ╥ Ӈ SSP
CNGB030299/HLA19061 01	B*15:27 B*38:02	B*15:27 B*38:02			
CNGB030307/HLA19069 02	B*13:01 B*35:03	B*13:01 B*35:03			
CNGB030295/HLA19057 03	B*15:11 B*51:01	B*15:11 B*51:01			
NGB030306/HLA19068 04	B*08:01 B*40:06	B*08:01 B*40:06			
CNGB030290/HLA19052 05	B*52:01 B*58:01	B*52:01 B*58:01			
CNGB030125/HLA18005 06	B*13:02 B*15:02	B*13:02 B*15:02			
CNGB030315/HLA19077 07	B*13:01 B*58:01	B*13:01 B*58:01			
CNGB030122/HLA18002 08	B*27:05 B*48:01	B*27:05 B*48:01			B*27:05
CNGB030153/HLA18024 09	B*27:05 B*44:03	B*27:05 B*44:03			B*27:05
CNGB030150/HLA18021 10	B*27:05 B*58:01	B*27:05 B*58:01			B*27:05

3

ɲ Ъ PCR HLA B27 ε í [12 14] ̓Ӈ ϒ í ̓Ӈ ˀA Ă ğ ɟ ˀ ↀ Δ ˀ ̓Ӈ ğ ϫ ğ ۷ Ψ ƒ ˘ ↀ Δ ל ɨ ˀ ̓Ӈ ï ˀA ɔ ۸ ל ɨ ' w ˀ m ɵ ɟ ˀA Ė m ϫ ₱ ΄Y

MLPA

˚ ˝ MLPA У І ЯІ Л
´ в ^ У ŏ У К ę ε К / w˚ ŧ
У ˀ ę DNA MLPA P036 ϕP070 Ξ Y ˈĦ І
ЯІ Л ´ в ^ ŏ ŧ Ă 774 ˁ
' ε 98.97% 766/774 Ό 52.09% 399/774 ę Ψ І ЯІ Л 50.26% ىي ε
47 XN +16 ę ε 47 XN +22 / 45 XO ˚ ' Ό І ╥ І в І ᾰ с І в ´ І в
І ŏ / І ŧ ŧ Ђ 20 / Ђ 35 Ψ У N<0.05 ŧ
^ Ђ 12 ^ У Ψ І Ό Ђ 12 ^ І Ό N<0.05 ŧ
І Л У К ę І Л ىي ЯІ ŧ ŋ /
І Л ŧ
У І Л ˚ ˝

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ABSTRACT Objective Using a multiple ligation dependent probe amplification method MLPA to detect chromosomes in abortive embryos and the genetic etiology of abortion was analyzed in combination with maternal age gestational age to assist in further genetic counseling. Methods The villus tissue samples of spontaneous abortion embryos in early pregnancy were collected and genomic DNA was extracted and tested using two kit probes MLPA P036 P070 combined with further analysis of statistics such as age and gestational age. Results A total of 774 samples were collected in this study with a detection success rate of 98.97% 766/774 and an abnormal detection rate of 52.09% 399/774 . The chromosomal aneuploidy anomaly was 50.26% the karyotype 47 XN +16 were the most common. Chromosomal monomer chromosome trisomes chimeras other complex aneuploids deletion/duplication chromosomes and other chromosomal abnormalities were detected. Pregnant women have higher abortion rates in the age group of less than 20 years

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ŏ ŏ [3] ɟ φ ٦
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l Ь Á К ŏ
˚ ෂ multiple
ligation dependent probe amplification MLPA
ң в— Ὼ ң в Ύ
вÃ ė MLPA ’ ѡ Θ ε
У К [5] ɟ
MLPA У l ŏ
У l Ỹ [m] ŏ
ę Ặ ĭ ė ε [m] К ٨ w ˚ ɟ

1

1.1

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φ ´ в HCG
ш Ǐ
ɔ У l я l ɟ
19~44 ج 31.7±5.9 ٧ ε 5
٧ 0 ~15 ٧ 3 ɟ

1.2

1.2.1 У ת ė DNA ٦
; 5~10 mg ḭ
ס ٦ ת ė DNA ɟ ASP 2680 ŏ
Ѧ DNA A260/A280 ğ 1.6~1.9 φ
ε 20~30 ng/ L ɟ

1.2.2 MLPA
P036 ٨ P070 Ḥ å̊ MRC
Honand ắ ˘ 23 l Ψ 13 ɑ14 ɑ15 l
2 Y Y l 1 Y ę
l в ˘ 2 Y ɟ ٦ DNA
~ Ь в P в ẇ PCR א ~ ٦ PCR
У
Coffalyser Ὸ Θ å̊ MRC ắ ˘ ŏ ɟ

1.2.3
SPSS 20.0 Θ ŏ Ὸ
ŏ % c^2
ŏ N<0.05 ε τ ɟ

2

2.1 MLPA

774 ʀ ’ 98.97% 766/774
8 ʀ ė ٦ DNA ٨
ɟ MLPA ה l 52.09%
399/774 ɟ ę Ψ l я l Ь ▌
50.26% ѡ 47 XN +16 ʀ ę ε 47
XN +22 ٨ 45 XO ˚ Ὸ l ╥ l
l א ɛ l ´ l ٨ ę l я l
Ь ğ ´ ىي l Ь Ψ ς ẇ 16 ɑ22 ٨ X
l l ŏ ▌
1.31% ɟ 1 ɟ

2.2 ˚ У l Ỹ

ğ Нь 20 ٨ Нь 35 ę У
Ψ l Ὸ N : 0.05 ğ
35 У Ψ l Ὸ
66.53% ɟ l я l Ь ẇ ŏ
l я l Ь У Нь 35
ẇ l У Ὼ
Нь < 35 ɟ 2 ɟ

2.3 ˚ ٧ У l Ỹ

˚ ٧ ˘ У l Ỹ
3 ٧ <12 ٧ У ж Ψ l Ὸ
Нь 12 ٧ l Ὸ N : 0.05 <12 ٧
У ж ה Нь 12 ٧ У ж ” N : 3<< <<

1 MLPA n

Table 1 Analysis of MLPA test results of aborted embryos n

MLPA õ	ʒ	٩ <12 ٩ Ȯ	٩ 12 ٩ Ȯ	<35 Ȯ	35 Ȯ
47 XN +2	11 2.76	10 1.49	1 1.08	9 1.75	2 0.8
47 XN +3	6 1.5	6 0.89	-	4 0.78	2 0.8
47 XN +4	5 1.25	5 0.74	-	4 0.78	1 0.4
47 XN +5	5 1.25	5 0.74	-	4 0.78	1 0.4
47 XN +6	8 2.01	8 1.19	-	5 0.97	3 1.2
47 XN +7	9 2.26	9 1.34	-	7 1.36	2 0.8
47 XN +8	18 4.51	17 2.53	1 1.08	11 2.14	7 2.79
47 XN +9	5 1.25	5 0.74	-	-	5 1.99
47 XN +10	6 1.5	6 0.89	-	5 0.97	1 0.4
47 XN +11	6 1.5	6 0.89	-	2 0.39	4 1.59
47 XN +12	2 0.5	1 0.15	1 1.08	1 0.19	1 0.4
47 XN +13	21 5.26	17 2.53	4 4.3	15 2.92	6 2.39
47 XN +14	13 3.26	11 1.63	2 2.15	6 1.17	7 2.79
47 XN +15	27 6.77	24 3.57	3 3.23	11 2.14	16 6.37
47 XN +16	75 18.8	68 10.1	7 7.53	51 9.94	24 9.56
47 XN +17	4 1	4 0.59	-	2 0.39	2 0.8
47 XN +18	9 2.26	6 0.89	3 3.23	4 0.78	5 1.99
47 XN +19	1 0.25 0.25	1 0.15	-	-	1 0.4
47 XN +20	11 2.76	8 1.19	3 3.23	5 0.97	6 2.39
47 XN +21	28 7.02	24 3.57	4 4.3	11 2.14	17 6.77
47 XN +22	45 11.28	43 6.39	2 2.15	21 4.09	24 9.56
45 XO	39 9.77	31 4.61	8 8.6	32 6.24	7 2.79
45 XN 4	1 0.25	1 0.15	-	1 0.19	-
45 XN -21	2 0.5	2 0.3	-	-	2 0.8
48 XN +10 +11	1 0.25	1 0.15	-	-	1 0.4
48 XN +12 +16	1 0.25	1 0.15	-	-	1 0.4
48 XN +15 +16	3 0.75	3 0.45	-	1 0.19	2 0.8
48 XN +16 +22	2 0.5	2 0.3	-	-	1 0.4
48 XN +21 +22	1 0.25	-	1 1.08	-	1 0.4
48 XN +7 +8	1 0.25	1 0.15	-	1 0.19	-
48 XN +9 +15	1 0.25	1 0.15	-	-	1 0.4
48 XN +3 +5	1 0.25	1 0.15	-	1 0.19	-
48 XN +4 +21	1 0.25	1 0.15	-	-	1 0.4
48 XN +4 +22	1 0.25	1 0.15	-	-	1 0.4
48 XN +7 +20	1 0.25	-	1 1.08	1 0.19	-
48 XN +7 +21	1 0.25	1 0.15	-	-	1 0.4
46 XN +14 20	1 0.25	1 0.15	-	-	1 0.4
46 XN +10 20	1 0.25	1 0.15	-	-	1 0.4
46 X +15	1 0.25	1 0.15	-	-	1 0.4
46 X +21	1 0.25	1 0.15	-	1 0.19	-
46 X +22	1 0.25	1 0.15	-	-	1 0.4
46 X +3	1 0.25	1 0.15	-	1 0.19	-
47 XXY	1 0.25	1 0.15	-	1 0.19	-
49 XN +15 +21 +22	1 0.25	1 0.15	-	-	1 0.4
49 XN +7 +14+ 15	1 0.25	1 0.15	-	-	1 0.4
46 XN/47 XN +13	1 0.25	1 0.15	-	-	1 0.4
46 XN/47 XN +2	2 0.5	2 0.3	-	1 0.19	1 0.4
47 XN +9/48 XX +7 +9	1 0.25	1 0.15	-	-	1 0.4
Yp11.31	1 0.25	1 0.15	-	1 0.19	-
8p23.3	1 0.25	1 0.15	-	1 0.19	-
6q27	1 0.25	1 0.15	-	1 0.19	-
2q37.3	1 0.25	1 0.15	-	1 0.19	-
1p36.33	1 0.25	1 0.15	-	1 0.19	-
18q11.32	1 0.25	1 0.15	-	1 0.19	-
17p13.3	1 0.25	1 0.15	-	1 0.19	-
15q26.3	1 0.25	1 0.15	-	1 0.19	-
14q32.33	1 0.25	1 0.15	-	1 0.19	-
14q32.33	1 0.25	1 0.15	-	1 0.19	-
11q25 10p15.3	1 0.25	1 0.15	-	-	1 0.4
11q25 4q35.2	1 0.25	1 0.15	-	1 0.19	-
4p16.3 3q29 ε	1 0.25	1 0.15	-	1 0.19	-
18q23 6q27	1 0.25	1 0.15	-	1 0.19	1 0.4
´	399 100	358 53.19	41 44.09	232 45.22	167 66.53

2

Table 2 Chromosomes of aborted embryos in different age groups

	l	l		l
		ʒ ʒ	Ȯ %	%
<20	58	43	74.14	10.78
20~25	86	42	48.84	10.53
25~29	142	39	27.46	9.77
30~34	227	105	46.26	26.32
35~39	165	z105	63.64	26.32
>40	86	62	72.09	15.54
N e			0.05	0.05

3

Table 3 Chromosomes of aborted embryos in different gestational weeks

ヽ	l	l	Ȯ	▌
		ʒ	%	%
<12 ヽ	673	357	53.05	89.47
12 ヽ	93	42	45.16	10.53
N e			0.05	0.05

3

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l 7 8 ɟ MLPA ğ

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ה 61% l Ȯ

9 ’ ɻ ε l ˝ˆ ɟ

ה l ʁ l ל ▌ l

96.49% ẇ 47 XN +16 ε ę ε 47

XN +22 ヽ 45 XO ɕ ▌ ʁ l

41.30% ˆ ה l ╥ l в l אָ ɕ l в

´ l ヽ ę l ʁ l ל ɟ

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ˆ ŏ 10 ¯ 0~8 Ă ~ ˆ R /R

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1 IGD/?
9

Ж ŏ 1 ϧ IGD/? ﻍ ﻧ ﻝ I Ж Ὼ
9 ﻱ Ɑ ﻍ ɻ ã ﻍ ﻧ ṿ ├ 5 ה ‴
Ǝ ṿ Ш ~ Sanger Ш ŏ ɻ *KIF1A* ﻍ ﻧ ﻝ Ң ṿ
I Ὼ 9 ﻱ Ɑ ﻍ ặ Ъ *KIF1A* ﻍ ﻧ m Y ה Ң c.914C>T
p.Pro305Leu τ ﻝ ɻ Ъ ã Ặ Ÿ Ъ *K1F1A* ﻍ ﻧ
ﻝ ﺍ ﻱ ˀ ה m Y Ж ﺍ Ψ ' ˀ ﺋ Y Ж ﻍ ɻ
q ḧ m q n m Ὼ 9 ﻱ MRD9 *KIF1A* ﻍ ﻧ _ r I s ư K c b g Ç Ὸ ▼ ˀ

KIF1A

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Yuneﻣﻣ B

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nant mental disorder type 9 MRD9 m
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ה Ⱦ *KIF1A* ﻧﺣ ﻍ Ⱨ Ⱦ
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A ᵰ B ṿ l ṿ 4 7 Y ɟ

1 9 MRD9

Figure 1 Physical features of patient with mental retardation autosomal dominant 9 MRD9

1

1.1

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ה Ἇ ɟ
Ἇ ~ ṿ ã ɟ ṿ
G3P2 2014 10 ﻧﺋ Ὶ ⊥ ﻧﺻ ד ├ Ὸ ɟ ẹ
Ю У ᾥ m Ὺ ﻧﺋ 41 ɻ У ɟ ṿ Ὸ
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12 Y Ὸ 12 Y ж ц 4 7
Y ‾ Ж в ╥ Ξ ɕ Y ɟ
Ю Ặ Ⱪ ´ ṿ вΞ Y ç
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1.2

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Ж ŏ ˀ ɟ ж ẇ ẹ в ۱ ɟ ‖ J ћ ε
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+ ƚ CNV ɟ ɟ ћ 2 ɟ
Ẉ Ẉ ẇ ẹ ۷ ˥ ג غ
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‘ IIlumina Novaseq6000 USA ж ã
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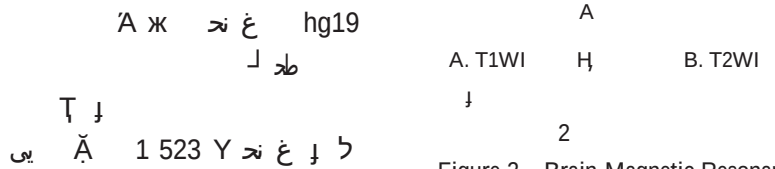

A. T1WI Ң B. T2WI Ң ɟ C. ط
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Figure 2 Brain Magnetic Resonance Imaging data of the proband

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Ă ג غ *KIF1A* c.914C>T p.Pro305Leu NM_
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ג غ ƚ Ң *KIF1A* c.914C>T p.Pro305Leu
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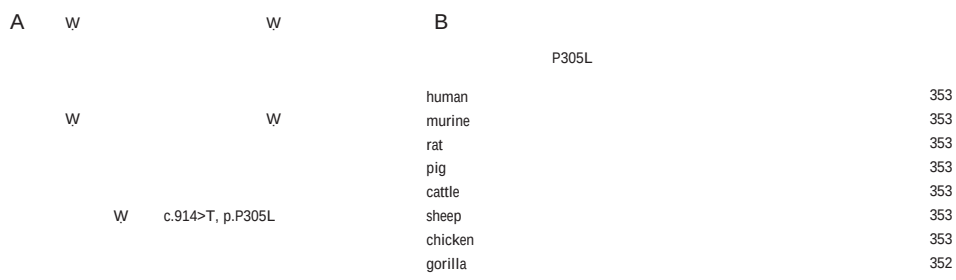

Figure 3 Sanger sequencing results of proband family and IGD/? gene p.P305L amino acid sequence of different species

KIF1A MRD9 OMIM MRI MDR9 *KIF1A* *KIF1A* MRD9 *KIF1A* *KIF1A* MRD9 Hamdan et al 2011 p.T99M Thr99Met *KIF1A* *KIF1A* MD EGFP *KIF1A* *KIF1A* *MYT1L* exon 15 6 Y WES

1 Yoshikawa K Kuwahara M Saigoh K et al. The novel de novo mutation of KIF1A gene as the cause for Spastic paraplegia 30 in a Japanese case J . eNeurological Sci 2018 14 34 37.

2 Pennings M Schouten MI van Gaalen J et al. KIF1A variants are a frequent cause of autosomal dominant hereditary spastic paraplegia J . Eur J Hum Genet 2020 28 1 40 49.

3 Van Beusichem AE Nicolai J Verhoeven J et al. Mobility Characteristics of Children with Spastic Paraplegia Due to a Mutation in the KIF1A Gene J . Neuropediatrics 2020 51 2 146 153.

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CTCs cfDNA

CTCs ɷ DNA cfDNA ᵴ ŧ Ψ ɵ

ᵉ ɟ ˥ 2014 4 2016 4 ŧ 163 ʒ ẹ Ψ 85 ʒ ˜

ε ŧ ŧ Ɠ 78 ʒ ε ŧ ˀ ⁿ ˀ Ấ ǀ ɾ 50

ʒ ɟ ˘ CTCs œfDNA ẇ Ⱪ CA125 œCA153 ẇ CEA ɔ

Ə ROC ɔ ₸ ẇ ˊ ŧ ɵ ᵉ ˀ ŏ CTCs œfDNA

Á ŧ í ẇ ˜ Ặ _œfG A

3 0 $ شم Q f•@ö•Añ ƯŽ ˆD°H2¯Á5 / a°ØQ ‘ A: àÎ z 3 0 $ $ & (aðFi i Ð" s ##sY $ & (T D G aP/

CTCs in breast cancer patients with tumors not smaller than 2 cm was higher than that with tumors smaller than 2 cm the differences were statistically significant N : 0.05 . The positive rate of cfDNA in patients with lymph node metastasis was higher than that without lymph node metastasis the differences were statistically significant N : 0.05 . At 3 years after surgery positive rates of CTCs and cfDNA in the disease progression group were higher than those in the disease non progression group N<0.05 . Conclusion Blood CTCs and cfDNA detection have high diagnostic value for breast cancer and are closely related to the clinical pathological characteristics and prognosis of patients.

KEY WORDS Circulating tumor cell Circulating free DNA Traditional tumor marker Breast cancer

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H [1] ɟ ہ † ה ς ; ΄Y ה ∖ ɔ † O ɾ Ỹ [2 3] ɟ † ה ل O ɟ ė † ל ה ώ̓ ├ ﷺ Ặ ɟ ζ εm 3 ḡ † B ϑ† ϑ Ǻ ж щ Ə ϑ ὰ ϑθ Ỻ [4] ɟ ہ í ɔ National Academy of Clinical Bio chemistry NACB ├ ┸

Ɑ 125 carbohydrate antigen 125 CA125 ϑ

Ɑ 153 carbohydrate antigen 153 CA153 ẇ

Ɑ carcino embryonic antigen CEA

Нь † [5] ɟ ŭ ה circulating tumor cells CTCs ϑ DNA circulating free DNA cfDNA ğ Ψ Ə ε [6] ɟ ğ CTCs œfDNA ´ ğ † Ψ ϑ e ŭ CTCs ϑ cfDNA Ά í ẇ ~ Ặ ɟ

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ך 2014 4 2016 4 † 163 ϛ ę Ψ 85 ϛ ~ ε † † Ɒ 78 ϛ ε † ˀ n ˀ Ả l ɾ 50 ϛ ɟ † ڜ 45.46± 11.62 ڜ 43.29±12.73 ڜ 46.35±10.58 ɟ 3 τ N<0.05 Ė ’ ɟ Ả Ỻ † ~ ΄Y ε ϑ╥´ ה Ė ˀ Ш ɟ Ỻ ώ̓ ɔ ɔ ϑỈ ŭ ´ ę ђ O ϑ ϑ ' ˝ ã ´ Ό ğ O Нь �://ð † ğ ɟ Ң ׀ Ж Ỻ ˇ ɔ ڜ ˀ Ш ɟ

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1.2.1 ϛ ẇ

ɔ m ж İ ׀ Ặ ɔ ; 5 mL ~ ɟ

1.2.2 CTCs

ẍ Ψ ẉ Ɑ Ң P Ő ẍ ẉ Ң CTCs ~ ẉ ; CTCs ׀ ó ɟ ó Ỻ w 2 Y CTCs/3.2 mL ε í e ṽm ת ´ >2 Y Ɑ ’ ε 1 Y >1 Y ◑ ε [7] ɟ

1.2.3 cfDNA ϑ

ŭ ל QIAGEN ڊ ė DNA ɔ Ḥ ˝ 51106 Ш Ə ך DNA ẉ PCR DNA ˉ ɟ ę Ψ GADPH ɔ 5′GGAAGGTGAA GGTCGGAGTC3′ ; 5′GAAGATGGTGA TGGGATTC3′ Ώ 5′FAM CAAGCTTCC CGTTCTCAGCC TAMRA3′ ɟ w 1×10³ ڊ ė ε Ỻ [8] ɟ

ã ɔ ה ẉ ẍ ŭ Ѧ Ψ CA125 ϑCA153 ẇ CEA ę Ψˇ Ỻ ε CA125>35 U/mL CA153> 31.5 U/mL CEA>5 U/mL ´ ṽm ◑ ε [9] ɟ

1.2.4 ~

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2019 4 30 Ỹ

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Ə ε Ξ CTCs œcfDNA

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Ξ Ξ SNK o w l

% c^2 ɔ Ə

receiver operating characteristic ROC

CTCs œcfDNA Ꮒ † ’ w ;

area under the curve AUC ę

ɵ e X w N : 0.05 ε

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2.1 ˘ CTCs ɷcfDNA ɷCA125 ɷCA153 ẇ CEA

˘ CTCs ɷcfDNA ɷCA125 ɷCA153 ẇ CEA ☪ τ N<0.05 ę Ψ † ɔ Ꮒ ɻ Ė τ N<0.05 ӂ ɻ τ N<0.05 1 ɟ

1 CTCs cfDNA CA125 CA153 CEA $\bar{x} \pm s$

Table 1 Comparison on levels of serum CTCs cfDNA CA125 CA153 and CEA among all groups $\bar{x} \pm s$

	† I=85	I=78	I=50	D e	N e
CTCs Y	1.34±0.29[ab]	0.03±0.01	0.00±0.00	1325.262	<0.001
cfDNA ×10³ نز غ	29.65±8.57[ab]	0.05±0.01	0.03±0.01	762.096	<0.001
CA125	22.37±7.24[ab]	16.21±5.20	15.43±4.67	29.931	<0.001
CA153	35.84±11.62[ab]	9.13±2.65	8.87±2.41	316.891	<0.001
CEA	6.69±2.13[ab]	1.85±0.54	1.76±0.42	309.314	<0.001

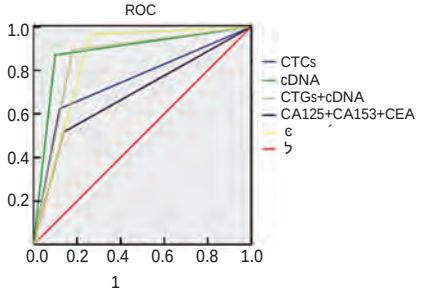
Ά [a]N : 0.05 Ά [b]N : 0.05 ɟ

2.2 CTCs œcfDNA † ROC ŏ Ė τ N<0.05 ӂ cfDNA ROC ŏ CTCs œcfDNA ₸ ´ ẇ ɕ NA ɷCTCs+cfDNA ẇ ɕ ´ Ξ Ξ AUC ´ † AUC Ꮒ Ⱪ τ N<0.05 ɟ 2 ɷ๑ 1 ɟ

2 CTCs cfDNA

Table 2 Diagnostic efficiency of serum CTCs cfDNA and traditional tumor markers

	AUC	73#AG	%	%
CTCs	0.752	0.668~0.835	62.40	88.00
cfDNA	0.885	0.822~0.949	87.00	90.00
CTCs+cfDNA	0.857	0.784~0.930	89.40	82.00
CA125+CA153+CEA	0.689	0.599~0.779	51.80	86.00
ɕ ´	0.852	0.775~0.930	96.50	74.00



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1 CTCs cfDNA ROC

Figure 1 ROC curves of serum CTCs and cfDNA in the diagnosis of breast cancer

2.3 CTCs œcfDNA Ά † í Ą

2 cm † CTCs Ꮒ <2 cm Ė τ N< 0.05 CTCs ğ ˝ ɷ ی ɷ Ỹ ɷTNM ŏ ɷŏ ɔ ɷ τ N<0.05 cfDNA Ꮒ Ė τ N : 0.05 cfDNA ğ ˝ ɷ ی ɷ Ỹ ɷ ɷTNM ŏ ɷŏ ɔ

τ N<0.05 22 ϡ Ὸ ϡ Ὸ ƿ˜ ƿ˜

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2.4 CTCs ȼcfDNA Ä † ˜ Ą

2019 4 30 85 ϡ † ˜

3 CTCs cfDNA l %

Table 3 Relationship between serum CTCs cfDNA levels and clinicopathological features of breast cancer patients l %

		l	CTCs	c^2 e	N e	cfDNA	c^2 e	N e
	40	26	15 57.69	0.591	0.898	21 80.77	0.228	0.973
	41~50	34	21 61.76			29 85.29		
	51~60	19	13 68.42			16 84.21		
	60	6	4 66.67			5 83.33		
ي		48	31 64.58	0.803	0.669	42 87.50	1.347	0.510
	˜	17	9 52.94			13 76.47		
		20	13 65.00			16 80.00		
Ỹ		22	14 63.64	0.021	0.885	19 86.36	0.173	0.677
		63	39 61.90			52 82.54		
cm	2	42	31 73.81	4.642	0.031	36 85.71	0.288	0.591
	<2	43	22 51.16			35 81.40		
TNM ŏ		19	9 47.37	2.932	0.402	15 78.95	0.552	0.907
		36	23 63.89			30 83.33		
		21	14 66.67			18 85.71		
		9	7 77.78			8 88.89		
ŏ ɔ	ɧ ŏ ɔ	18	14 77.78	3.702	0.157	17 94.44	2.769	0.250
	Ψ ŏ ɔ	22	15 68.18			19 86.36		
	ŏ ɔ	45	24 53.33			35 77.78		
		31	22 70.97	1.543	0.214	30 96.77	6.222	0.013
		54	31 57.41			41 75.92		

ɔ w ’ ˚ ɟ ж ѿ CTCs œfDNA
† e ˈY τ
˚ Б ɔ ﾑ ŏ ę í
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1 Salatino M Girotti MR Rabinovich GA. Glycans pave the way for immunotherapy in triple negative breast cancer J . Cancer Cell 2018 33 2 155 157.
2 Desantis C Ma J Bryan L

VEGF IL 18 MCP 1

ŏ ѽ PE VEGF ⊕L 18 ⊕MCP 1 ѭ Ά Ь Ặ
ɟ ŏ Нь 2017 2 2020 2 í 118 ҳ PE í ę ŏ ε
PE 63 ҳ ⊕PE 55 ҳ ɟ ҷ ٦ 60 ҳ ҷ Ə ε
3 ж VEGF ⊕L 18 ⊕MCP 1 ѭ Ь ŏ ę Ặ ɟ PE
Ỉ ἐ VEGF в ч 18 IL 18 ⊕╥ ɔ 1 MCP 1 Нь PE
ѭ Ė τ N<0.05 PE ⊷
AA в ♥ HCT ⊕D J I D D Нь PE ѭ AA ⊕HCT ⊕D D PE . 3

were observed in the three groups and their correlation was analyzed. Results Serum vascular endothelial growth factor VEGF interleukin 18 IL 18 monocyte chemoattractant protein 1 MCP 1 levels of patients in the severe PE group were significantly higher than those in the mild PE group and the control group N<0.05 . The levels of arachidonic acid induced maximum platelet aggregation rate AA hematocrit HCT and D dimer DD of patients in the severe PE group were significantly higher than those in the mild PE group and the control group. The levels of AA HCT and D D increased with the severity of the disease and the difference was statistically significant N<0.05 . Correlation analysis showed that AA HCT D D VECG IL 18 and MCP 1 were all positively correlated N<0.05 . Conclusion As the disease progresses in patients with preeclampsia serum VEGF IL 18 MCP 1 levels increase. VEGF IL 18 MCP 1 and hemorheological indicators are positively correlated which can be used to judge the condition of patients with preeclampsia Predictive indicators.

KEY WPRDS Pre eclampsia Hemorheology indicators Monocyte chemoattractant protein 1 Vascular endothelial growth factor Interleukin 18

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ε 8%~13% ğ ₔ ה ε 9.5%~10.5% [1] ɟ

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ẇ H ζ Ɑ ė ɟ ώ pre eclampsia

PE У φ[m] w Ὸ ♥ в

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PE ' ŏ ε PE ۱ PE PE ‴ ẇ

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PE ה Ą ӂ Ə ε ṿ ●

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ğ[m] [3] ɟ PE ה Ψ ﬧ

ğ א ч 18 interleukin 18 IL 18

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[5] ɟ ė ŏ PE

VEGF ɞIL 18 ɞMCP 1 ẇ Ά Ɩ Ą

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ך 2017 2 2020 2

118 ҂ ώ O ŏ ε PE

I=63 ẇ PE I=55 ɟ ẹ Ψ

PE ĂA ε 20 ۷ ~ Ὸ ♥ 140/90

mmHg в 300 mg/24 h ˀ ¥

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20 ۷ ~ Ὸ ♥ 160/110 mmHg в 2.0/

24 h в ╗ в ᵀE

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1 3 $\bar{x}\pm s$

Table 1 Comparison of general information of 3 groups of patients $\bar{x}\pm s$

ą̈	I		۷ ۷	BMI kg/m²
PE	63	27.19±5.32	34.15±3.79	24.22±3.17
PE	55	27.56±5.47	34.75±3.42	24.51±3.03
	60	27.89±5.75	34.52±3.73	24.14±3.19
D [e]	-	0.25	0.41	0.22
N [e]	-	0.780	0.666	0.803

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1.2.1 VEGF ɞIL 18 ɞMCP 1

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ʄ ẍ Ⴘ Ψ VEGF ɷIL 18 ɷ
MCP 1 Ḥ ă ˘
w Y O Ḥ Ш
Ὸ Δ ж Ⴘ Ə ɟ
1.2.2 ƾ
Ᵽ ᶁ
arachidonic acid AA ɷ ♥
hematocrit HCT ɷD J l D Dimer D D ɟ ẹ
Ψ AA Ꮯ w Ⱥ ƚ ε ₔ Sigma ă ˘
SC 2000 ىي ˝ 4 Ⱥ HCT ←
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30 min ♥ e D D Ꮯ w ẍ
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1.3
˘ ɔ VEGF ɷIL 18 ɷMCP 1
Ỹ w ẇ ƾ ŏ VEGF ɷ
IL 18 ɷMCP 1 Ά ƾ Ặ ɟ
1.4
SPSS 18.0 Θ ŏ
$\bar{x}\pm s$ D
l % c^2 Ặ ŏ
Spearman Ặ ŏ ɟ w N<0.05 ε Ė
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2.1 3 VEGF ɷIL 18 ɷMCP 1 Ỹ
3 VEGF ɷIL 18 ɷMCP 1 PE
>PE > τ
N<0.05 ɟ 2 ɟ
2.2 ˝ ж ƾ
3 ж AA % ɷHCT % ɷD D g/mL
PE >PE >
τ N<0.05 ɟ 3 ɟ

2 3 VEGF IL 18 MCP 1 $\bar{x}\pm s$

Table 2 Expression of serum VEGF IL 18 and MCP 1 in the 3 groups $\bar{x}\pm s$

ά	l	VEGF ng/L	IL 18 pg/ml	MCP 1 pg/mL
PE	63	126.45±29.41	167.16±20.75	267.05±37.56
PE	55	162.05±50.24	194.05±17.42	422.04±53.01
	60	39.16±8.41	103.15±27.01	140.26±20.46
D e		210.28	258.33	756.28
N e		0.000	0.000	0.000

3 $\bar{x}\pm s$

Table 3 Hemorheology indexes of different population $\bar{x}\pm s$

ά	l	AA %	HCT %	D D g/mL
PE	63	57.06±7.05	0.35±0.03	1.21±0.26
PE	55	73.47±8.48	0.38±0.05	1.98±0.21
	60	30.81±6.01	0.30±0.01	0.53±0.11
D e		515.76	84.19	724.59
N e		0.000	0.000	0.000

2.3 ŏ PE VEGF ɷIL 18 ɷMCP 1 ẇ Ά
ƾ Ặ
Ặ ŏ AA ɷHCT ɷD D ɷVECG ɷ
IL 18 ɷMCP 1 φ ڜ ε Ặ N<0.05 4 ɟ

3

˝ ẵ ה ε 1/200 ₔ
ė H ж 5 ˛ ж [7] ɟ PE Ə ε
O ה φ[m] Ϛ У ẇ م У ṿ H
ζ Ꭰ ġ φ[m] [8] ɟ PE ´ ˈ ڛ ẇ
ƾ ה ۊ ה ۅ ɷ
ɷ Ὼ ɷ ۅ [9] ɟ
[m] ה ۊ ˈ ~ Ấ
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4 PE VEGF IL 18 MCP 1

Table 4 Levels of VEGF IL 18 and MCP 1 in PE patients and their correlation with hemorheology indexes

	AA %		HCT %		D D g/mL		VEGF ng/L		IL 18 pg/mL		MCP 1 pg/mL	
	p e	N e	p e	N e	p e	N e	p e	N e	p e	N e	p e	N e
AA %	-	-	0.571	0.001	0.331	0.033	0.495	0.003	0.943	0.000	0.834	0.002
HCT %	0.571	0.001	-	-	0.915	<0.001	0.413	0.005	0.392	0.003	0.765	0.001
D D g/mL	0.331	0.033	0.915	<0.001	-	-	0.516	0.002	0.467	0.005	0.912	0.000
VEGF ng/L	0.495	0.003	0.413	0.005	0.516	0.002	-	-	0.685	0.007	0.864	0.002
IL 18 pg/mL	0.645	0.012	0.513	0.002	0.439	0.003	0.510	0.002	-	-	0.739	0.001
MCP 1 pg/mL	0.761	0.001	0.812	0.000	0.561	0.001	0.903	0.000	0.812	0.002	-	-

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ẇ Ặ PE

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Ỉ ɔ Ỉ [11] ɟ VEGF

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3…4 % qp ¯Dë*LSB ⇒SG ŒSG O B T Ð •BD@..tŠZ° ·ŒE!ŒÆRvÄQ'Š¥E!ąRAvgg B¤ŒE#ÔÑ¥R bMc#Ê¥ÁÊÊÊ

sFGL2

ө ф ىى CHB ٧ Ψ ' ч 2 sFGL2
ί τ ɟ ٦ ٹ 140 ٶ CHB Ə ε ф ىى CHB ę Ψ 25
ٶ CHB ٦ ̂ Γ ىى 42 ٶ Ə ε Γ ىى
CHC ٦ ̂ l ғ ж 68 ٶ ɟ ÿ ٧ ˘ sFGL2
´ א ˘ ٧ Ψ qDEJ0 mRNA ⱵⱭ ٹ ˘ Spearman ŏ
ⱵⱭ Ά CHB ˘ ί Ặ ɟ ٹ 3 ~ Ő sFGL2 ١ ٧
Ψ qDEJ0 mRNA ⱵⱭ ѽ˜ ɟ CHB sFGL2 ١ qDEJ0 mRNA
ҷ Ҥ CHC ١ Ė τ N<0.05 CHC ١ sFGL2 ١ qDEJ0
mRNA τ N>0.05 ɟ Spearman Ặ ŏ sFGL2 ١ qDEJ0 mRNA
Ά HBV DNA ɵALT ɵAST ٧ Ặ N<0.05 Ά GGT ɵT Bil ɵAFP Ặ N>0.05 ɟ ~
sFGL2 ١ qDEJ0 mRNA ѽ ҷ ; Ė τ N<0.05 ɟ CHB
sFGL2 ٦ Ά HBV DNA ɵALT ɵAST 'Y Ặ ~ sFGL2 ; ɟ
' ч 2 ф ىى ÿ ٧ ´ א

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ABSTRACT Objective To evaluate the clinical value of soluble fibrinogen like protein 2 sFGL2 in peripheral blood of patients with chronic hepatitis B CHB . Methods Enzyme linked immunosorbent assay and real time fluorescent quantitative PCR were detected the levels of plasma sFGL2 and qDEJ0 mRNA in peripheral blood of 140 CHB patients CHB group in which 25 cases were treated with antiviral drugs antiviral group ɵ42 HCV patients CHC group and 48 healthy cases control group comparing the differences among those groups Spearman correlation was analyzed between sFGL2 level and clinical indexes in CHB patients estimating the differences in the levels of plasma sFGL2 and qDEJ0 mRNA before and after antiviral treatment in antiviral group of 25 cases. Results The levels of plasma sFGL2 and qDEJ0 mRNA in the CHB group were higher than those in the CHC group and the control group the difference were statistically significant N<0.05 no statistical difference between the CHC group and the control group in plasma sFGL2 and qDEJ0 mRNA N>0.05. Spearman correlation analysis showed that sFGL2 concentration and qDEJ0 mRNA expression were positively correlated with HBV DNA ALT and AST N<0.05 but not correlated with GGT T Bil and AFP N>0.05 . The concentration of sFGL2 and the expression of qDEJ0

mRNA after antiviral treatment were significantly lower than before antiviral treatment and the difference was statistically significant N<0.05 . Conclusion SFGL2 is significantly increased in CHB patients which is closely related to the abnormalities of HBV DNA load ALT and AST and sFGL2 is significantly decreased after antiviral treatment.

KEY WORDS Soluble fibrinogen like protein 2 Chronic hepatitis B ELISA qRT PCR

’ ч 2 soluble fibrinogen like protein 2 sFGL2 ɑ Ă Ά ɑ ۱ ˀ ę ᴝ ɛ́ Ң Њ 7q11.23 ã 7 kb ˉ 2 Y 1 Y Ỉ ˉ [1] ɟ sFGL2 ζ T ŏ Ə ε ӧ Ă ɛ́ ’ Ă T ۱ ч B ɛ̌ H [2] ɟ ہ Ỉ sFGL2 Ά [3] ɞ ợ [4] ɞ [5] Ă ɟ sFGL2 ğ ת Ă Ψ Ə ɔ ą̃ ж ζ ѡ ε ζ [6 7] Њ ŏ sFGL2 ƙ ɔ ѡ í τ Ά í Ă Ă ŏ ğ ę CHB í ۱ ~ ɵ e ˀ Ả sFGL2 ğ CHB ѽ˜ ƙ ɔ ŏ ε CHB ’ ɟ

1

1.1 [m]

ך 2019 8 1 ~2020 1 22 ğ CHB 140 ϛ Ə ε ф ى CHB 86 ϛ 54 ϛ ᴝ 38.96±12.07 ɟ ę Ψ 25 ϛ CHB ˇ í 16 ϛ 9 ϛ ᴝ 40.65±13.41 ɟ ך ˀ Г ى 42 ϛ Ə ε Г ى CHC 35 ϛ 7 ϛ ᴝ 40.95±6.24 ɟ Ɠ ך ˀ l ғ ж 68 ϛ Ə ε 26 ϛ 42 ϛ ᴝ 36.71±12.85 ɟ ˘ τ D=2.492 N=0.116 Ė ’ ɟ Ả ˜Ă ŏ ą́ ´ Ψ ╞ ├ Ж Ж ŏ Ж ۱ Ψ ╞ ├ Ж ŏ Ж Ă ф ى ≟ 2019 [8] ф ى ≟ 2019 [9] ˜Ă ɟ ˜Ă ф ѡ Г ך ´ ę ђ ´ ę ђ ę ђ ɔ ɔ ’ ‴ ã ɟ ғ l ɟ ƙ Ά ѽ ᴝ ˀ Ш Ң ۱ Ж ˜Ă ɟ

1.2

1.2.1 ѡ

ɔ 5 mL Њ ф J ظ ф J ˝H Ψ Њ 3 Y ˜ Ɠ 5 mL Њ ф J ظ ф J ˝H Ψ ɟ ˜ 30 min Ỉ ך ã 1.5 mL Њ Ψ ж ۱ ŏ Й ɔ Ш ך ɔ ۱ ╥ Y -80 ך ‴ æ ã 1 500 rpm 20 min ŏ -80 ך ɟ

1.2.2 ӧ ۱ sFGL2

ж ’ ч 2 sFGL2 Ң ă ˘ Ш ɔ Ψ sFGL2 CHB ˀ ├ HBV DNA ɞ Г ala nine aminotransferase ALT ɞ aspartate aminotransferase AST ɞ gluta myl transferase GGT ɞ total bilirubin T Bil ۱ alpha fetoprotein AFP ɟ

1.2.3 ´ א qDEJ0 mRNA

Trizol Invitrogen ہ ך ۱ ╥ Y RNA˜ א ε cDNA ɟ ѡ cDNA ε sFGL2 F AGGCAGAAACGGACT GTTGT sFGL2 R CCAGGCGACCATGAAGTA CA ھ ѡ GAPGH GAPGH F TGCAC CACCAACTGCTTAGC GAPGH R GGCATG GACTGTGGTCATGAG ε Ỉ ƙ ɟ l ; SYBR™ Premix 10 L Forward primer 10 pmol/ L 2 L Reverse primer 10 pmol/ L 2 L cDNA 3 L H_2O 8 L ɟ 95 ƙ 2 min ˜ ѡ ; Θ 40 Y 95 10 s 60 45 s ɟ 2 [Ct] ę ę Ψ CT=CT ע CT ا ט ע CT= CT CT ۰ ғ 3 ך ᴝ Ct e ɟ

1.3

SPSS 13.0 Θ ŏ

x̄±s Ξ r

D Ặ ŏ Pearson N<0.05 ε

τ ɟ

2

2.1 3 sFGL2 ۱ qDEJ0 mRNA

3 sFGL2 ۱ qDEJ0 mRNA

CHB >CHC >

τ N<0.05 ɟ 1 ɟ

1 3 sFGL2 qDEJ0 mRNA x̄±s

Table 1 Coparing the levels of plasma sFGL2 and qDEJ0 mRNA in 3 groups x̄±s

ậ	sFGL2 ng/mL	sFGL2 mRNA
CHB	93.59±38.96	63.44±38.96
CHC	26.08±5.14	12.09±6.70
	16.68±3.39	8.24±5.94
D e	193.449	102.275
N e	<0.001	<0.001

2.2 sFGL2 ۱ qDEJ0 mRNA Ά CHB

˘ í Ặ ŏ

Spearman ŏ sFGL2 Ά HBV DNA

ɷALT ɷAST ۷ Ặ N<0.05 Ά GGT ɷ

T Bil ɷAFP Ặ N<0.05 2 ɟ

í	sFGL2 p e	qDEJ0 § § N e
HBV DNA LogF	0.982	<0.001
ALT	0.336	<0.001
AST	0.346	<0.001
GGT	0.149	0.079
T Bil	0.045	0.595
AFP	0.005	0.954

2.3 ώ˜ sFGL2 ۱ qDEJ0 mRNA

3 Y ˜

sFGL2 ۱ qDEJ0 mRNA ώ

; ϑ τ N<0.05 3 ɟ

3

ώ ϕ ىی hepatitis B virus HBV

ẍ Ƙ Ặ щ ‴

T ẹ T regulatory

T cell Treg ğ ẹ ה ה Ψ Ặ Θ [10] ɟ

sFGL2 ζ T ŏ Treg

ˈ ‴ ’ ė ẹ ˈ

ε [11] Ά Ặ

Ϛ ẇ ẹ Ψ COLAK [12] sFGL2 ğ

Ψ AI [13] sFGL2

ğ ẍ ╗ ẹ ╗

Ά AIH O YU [14] ğ ה

Ψ sFGL2 ’ ا ל Ά ה

ɟ

sFGL2 ğ Ặ Ψ T Ė ‖

ŏ Θ ɟ ا sFGL2 ’

Ặ Tregs ɟ Th1/Th2

[15] ɟ ا Ǐ Ψ Foerster [16] ğ Γ ىی

۷ Ψ sFGL2 Ά ŏ ۱ ˜

ˈY Ặ א ۱ ɔ O ۷

sFGL2 ɟ sFGL2 Ά

ˈY Ặ ɟ Ὸ sFGL2 ɔ

ىی ŏ ל Ά HBV Ặ

T ˈ T

ẇ ẍ ɔ HBV ˜ ɔ ε CHB

Ặ ė φm [17] ɟ ɔ sFGL2 ’

Ặ Ъ ا Ь HBV T

ا У ẍ ɔ ъ ˛ HBV Ặ ۱

m ה ɟ ė sFGL2 ğ CHB Ψ ה ה

w ẇ í ŏ Ψ Θ e Ấ ɟ

Ѝ [18] sFGL2 ğ HBV DNA ‴

˛ Ặ sFGL2 Ά CHB

3 sFGL2 qDEJ0 mRNA x̄±s

Table 3 Coparing the levels of plasma sFGL2 and qDEJ0 mRNA befor and after antiviral treatment in 25 CHB cases x̄±s

	ا	ώ	˜	r e	N e
sFGL2	25	127.41±24.07	74.40±22.97	48.463	<0.001
qDEJ0 mRNA	25	97.26±12.38	25.72±12.52	22.068	<0.001

' 'Y Ą̌ ɟ 3 sFGL2 ƚ Á Ъ

ϛ Ъ Ї̆ ´ ' ɟ ġ

sFGL2 ' ε Ţ CHB O

ġ ' Ə ε CHB ɞ ƚ

ɔ ɞí ŭ̈ í Ə Ψ

ɟ

Ψ CHB 3 ~

sFGL2 ς ; Á ϒ [19] m

sFGL2 Á 'Y

Ą̌ ɟ ġ sFGL2 ' ε CHB

ɟ c Ћ sFGL2 ŭ̈ CHB

ϒ Ψ w ẇ ŏ̃ CHB

ѽ˜ ƚ ɔ ẇ ę Ą̈ ;[m]

HBV sFGL2 ġ ' w ẇ sFGL2

Ą̈ Tregs Ą̌ Ą̈ ɟ

ɔ sFGL2 Ə ε[m] ӧ ŏ̃ ŭ̈

CHB Ψ Ė ӧ Ə

ɟ ŭ̈ CHB ϒ Ψ Á

í 'Y Ą̌ ' Ə ε CHB ɞ ƚ ɔ ɞ

í ɟ̊ sFGL2 ŭ̈ CHB

˜ ; ς ' Ə ε CHB

ŭ̈ í Ə Ψ

ɟ

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ṭ ğ У ѽ à ϗ Ψ ı У ѽ ө e ɟ
ϖ 2017 1 2019 12 105 ϗ У ѽ à ϗ Ə ε Є
Ж ʎ ğ ˀ ˜ ṭ ы ŏ ɟ w í ε ΆA ṭ ы ŏ Ό
˘ ы ı 13 є ı ´ ѳ18 є ı ´ ѳ21 є ı ´ в ı Ў ẁ ˘ ы
ı ѳΆA в ɔ Ə ROC ẁ ROC ; AUC ŏ
ṭ ы ŏ ı ɟ 105 ϗ У ѽ à ϗ í ı 83
ϗ ę Ψ Ъ 13 є ı ´ 9 ϗ 18 є ı ´ 13 ϗ 21 є ı ´ 51 ϗ ı 10 ϗ w í
ε ΆA ṭ ы ŏ 13 є ı ´ ε 88.89% ΆA ε 96.19% ε
96.88% ṭ ы ŏ 18 є ı ´ ε 92.31% ΆA ε 99.05% ε 100.00%
ṭ ы ŏ 21 є ı ´ ε 98.04% ΆA ε 97.14% ε 96.30%
ṭ ы ŏ ı ε 90.00% ΆA ε 98.10% ε 98.95% ṭ ы ŏ
ı ε 95.18% ε 72.73% ΆA ε 90.48% ɟ ṭ NIPT
ж ı Ė У ѽ ө e ε Ђ Ђ в Ж ʎ w ’ Ь ɟ
ṭ à У ѽ ı ΆA

LIU Hui FANG Huiqin CHEN Wei YAN Yalan YUAN Jing
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ABSTRACT Objective To explore the value of amniocentesis in the prenatal diagnosis of chromosomal abnormalities in non invasive high risk cases of prenatal screening. Methods A total of 105 non invasive high risk cases of prenatal screening admitted to our hospital from January 2017 to December 2019 were selected as the research objects and genetic counseling was given. After the patient s informed consent amniocentesis karyotype analysis was performed. Based on the clinical follow up results statistical amniocentesis karyotype analysis was performed to detect various types of chromosomal abnormalities 13 trisomy syndrome 18 trisomy syndrome 21 trisomy syndrome sex chromosomes etc. and the sensitivity accuracy and specificity of diagnosing various types of chromosomal abnormalities. Receiver operating characteristic curve ROC and area under ROC AUC were used to analyze the efficacy of amniotic fluid puncture karyotype analysis for diagnosis of total chromosomal abnormalities. Results Among 105 non invasive high risk cases of prenatal screening there were 83 cases of chromosomal abnormalities in clinical

follow up including 9 cases of 13 trisomy syndrome 13 cases of 18 trisomy syndrome 51 cases of 21 trisomy syndrome and 10 cases of sex chromosome abnormalities. Based on the clinical follow up results the sensitivity of amniocentesis karyotype analysis for 13 trisomy syndrome was 88.89% the accuracy was 96.19% and the specificity was 96.88%. Amniotic fluid puncture karyotype analysis for the diagnosis of 18 trisomy syndrome had a sensitivity of 92.31% accuracy of 99.05% and specificity of 100.00%. The sensitivity of amniocentesis karyotype analysis for diagnosis of 21 trisomy syndrome was 98.04% accuracy was 97.14% and specificity was 96.30%. Amniotic fluid puncture karyotyping analysis had a sensitivity of 90.00% an accuracy of 98.10% and a specificity of 98.95% the sensitivity of amniocentesis karyotype analysis for diagnosis of total chromosomal abnormalities was 95.18% specificity was 72.73% and accuracy was 90.48%. Conclusion Amniotic fluid puncture has a high prenatal diagnosis value for chromosomal abnormalities in NIPT high risk populations and can provide a reliable reference for eugenics and postnatal care genetic counseling.

KEY WORDS Amniotic fluid puncture Non invasive prenatal diagnosis High risk Chromosome abnormality Sensitivity Specificity Accuracy

ھ Ὸ ’ Ẉ ỵ 20 ˛ ~30 ˛ Ẉ Ὸ ỵ 100 ˛ ˆ Ὸ ѥ ھ [1] ɟ l ỵ Ὸ ζ Ɑ ė ɸ[m] ’ Ὼ ң ; в ѥ вѥ в ΄Y ѽ l ỵ Ὸ˜ в Ж Ӄ в ė У ѽ Ά Ἇ Ὸ ж і τ [2] ɟ J ц ѥ à У ѽ Noninvasive prenatal test NIPT ğ ї ặ Ė l Ὸ ۱ ң ˆ ğ У ѽ ỵ l Ψ ặ Ə [3] ɟ ж Ь NIPT ɔ ặ в ỵ в ė ĭ Ѓ ң ї NIPT ж щ ṭ ɣ [m] [4] ɟ w w ṭ ε ł Ѓ Ń م NIPT в ṭ [m] w ї ε ṭ [5] ɟ Ь ṭ ğ NIPT ж Ψ ɵ [e] ۱ ; ɟ

1

1.1 [m]

ך 2017 1 2019 12 105 ҷ У ѽ à ҷ 20~45 ҕ 36.24±4.30 ۱ 13~20 ۱ ҕ 18.54±1.60 ۱ è У 63 ҷ У 42 ҷ ɟ Ң ۱ Ӂ Ѓ ҕ ṭ в’ ğ ɔ ṭ ’ Ш ɟ Ѓ ɔ У ѽ У ѽ à ɔ ṭ ’ ΄ ỵ Ѓ У ѽ à ж ɟ í ΄ Р ¨Н ’ Ẉ Ẇ У l >37.4 Ὸ ε˜ Ѓ ѽ 1 Ỉ ڑ ΄ l Ӕ ɟ

1.2

1.2.1 NIPT

5 mL 10 000 rpm 10 min ך Ψ DNA в PCR ھ J ц ɱ ŏ ặ˘ l Z [e] ɟ ę Ψ 13 ѳ18 ѳ21 ˝ l Z [e] ğ -3.0~3.0 م Ỉ ε ң Ὸ م ε ɟ ę ђ l ẇ l ˘ Ė l Ỹ Ə ε ѥ ۱ ɟ

1.2.2 ṭ ی ŏ

NIPT Є К ۱ ğ ˘ ~ Ь 18~30 ۱ ṭ ɟ ך 20 mL ŏ Ь Ξ Y Ỉ ; 2 000 rpm 7 min ך 0.5~1 mL Ь 25 mL T نج Ё Ψ نج Ё نح Ά ₱˜ نج Ё Ψ نج Ё 37 ѳ5% CO_2 9 10 d Ỹ نج Ё نح Ь ɔ вң в ز ѳ ۱ J ز ˜ G ; 20 Y

ŏ Ψ ŏ ┐4 Y ŏ ㄴ
ж Ж ₔ ↓ ˜ I Ά Ά IS
CN2013 ي ŏ ɟ Ấ ṭ ώ ۓ
ي ε Rh ẹ ɡ ε Rh ч Ấ
У ώ ṭ ˜ ◑ RhD ẍ ɟ

1.2.3 í
ε Ё ┐ Ẇ 2 Y ж ↓
У ˜ в У ϗ
ɱ ɟ

1.3
SPSS 22.0 Θ
w X±S r I %
c^2 ↄ Θ Receiver op
erating characteristic ROC Ẇ ROC ; Area un
der the curve AUC ŏ ṭ ي ŏ
I ɟ N : 0.05 ε τ ɟ

2

2.1 í
105 ϗ У ώ ὰ ϗ í
I 83 ϗ 79.05% ẹ Ψ Ƀ 13 ϵ I ´
9 ϗ 10.84% 18 ϵ I ´ 13 ϗ 15.66% 21
ϵ I ´ 51 ϗ 61.45% I 10 ϗ
12.05% ɟ

2.2 ṭ ي ŏ Ὸ˘ ي I
Ỹ
í 105 ϗ ṭ ي ŏ Ὸ˘
ي I Ỹ ɟ 1 ɟ

1 13 I=105

Table 1 Amniotic fluid puncture karyotype analysis detected 13 trisomy syndrome I=105

í	13 ϵ I ´			18 ϵ I ´		21 ϵ I ´			I		
	8	1	9	12	1	13	50	1	51	9	1	10
	3	93	96	0	92	92	2	52	54	1	94	95
	11	94	105	12	93	105	52	53	105	10	95	105

2.3 ŏ ṭ ي ŏ ˘ ي I ˘ I вЁА в
τ N<0.05 2 ɟ

w í ε Ά ṭ ي ŏ

2

Table 2 Amniotic fluid puncture karyotype analysis for diagnosis of various types of chromosomal abnormalities

I ŏ	%	Ά %	%
13 ϵ I ´	88.89 8/9	96.19 101/105	96.88 93/96
18 ϵ I ´	92.31 12/13	99.05 104/105	100.00 92/92
21 ϵ I ´	98.04 50/51	97.14 102/105	96.30 52/54
I	90.00 9/10	98.10 103/105	98.95 94/95
c^2 e	2.504	52.049	4.090
N e	0.475	0.562	0.252

= ж / ж + ˆ ж ×100% Ά = + / ϗ ×100% = / ϗ + ˆ ϗ ×100% ɟ

2.4 ṭ ي ŏ Ὸ I Ỹ
í Ὸ I 83 ϗ I
22 ϗ ṭ ي ŏ Ὸ I
85 ϗ I 20 ϗ ɟ 3 ɟ

2.5 ŏ ṭ ي ŏ I

w í ε Ά ṭ ي ŏ
I ε 95.18% ε
72.73% Ά ε 90.48%

3

Ж О ˚ І в ѵ
в О ´ ח
ŏ ● ж ˜А жк Нь
э ǧ ˙О ң Ά ^
’ ח ѡ ˝ ὰ У
ѽ Ї Ѳ 6 ɟ NIPT Нь ۷ Ψ
ѵ DNA Нь ф э m
ὰ У ѽ Ά Ж О ˝Е
Ъ NIPT Ỷ ı ḭ ’
m ң ὰ У ѽ 7 ɟ
21 с І ´ 21 ˝ І
І 60% ѵ ǧ Ỉ ◗ У
в ˜ в ח в0 ם Ѧ’ Ύ υ 5 ¤ А 5 ӈ ˝Е

Th1/Th2

Th1/Th2 Ά O ɞ Ϗ Ă ɟ
2017 10 2019 10 Ь ICU ɔ 62 ϛ 28 d˜ í
ŏ ε H 20 ϛ ϟ 42 ϛ ŏ ˆ Ь Ấ ICU ˆ 1 d Ấ ICU ˜ 1 ϐ ϑ14 d
Ξ ϟ Ψ Th1 IFN ⁺CD3⁺CD4⁺T ϣ Th2 IL 4⁺CD3⁺CD4⁺T
ϯ Th1/Th2 e ŏ Ξ Th1 ϐTh2 ϯ ϣ Th1/Th2 e ɟ ı ´
Ϗ ŏ ˆ Ϗ 24 ϛ ϟ Ϗ 38 ϛ ŏ Ξ Th1 ϐTh2 ϯ ϣ Th1/Th2
e ɟ ˜ 1 ϐ ϑ14 d Th1 ϯ ϣ Th1/Th2 e ϗ Ь H Ė
τ N : 0.05 Th2 ϯ Ά H τ N<0.05 ɟ Ϗ Th1 ϯ ϣ
Th1/Th2 e ϗ Ь Ϗ Ė τ N : 0.05 Th2 ϯ Ά Ϗ
τ N<0.05 ɟ Th1/Th2 e ɳ O ˜ ˙ ˀ
´ Ϗ ˛ Th1 ϡ Th1/Th2 ˜ Th1 ˜ ɟ
Th1/Th2 O Ϗ

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ABSTRACT Objective To explore the relationship between Th1/Th2 cell imbalance and disease severity lung injury in patients with sepsis. Methods Sixty two patients with sepsis who were treated in ICU of the hospital from October 2017 to October 2019 were divided into the death group 20 cases and the survival group 42 cases according to the clinical outcomes after 28 d of treatment. At 1 d before entering ICU and at 1 7 and 14 d after entering ICU contents of Th1 cells IFN ⁺CD3⁺CD4⁺ T lymphocytes and Th2 cells IL 4⁺ CD3⁺CD4⁺T lymphocytes in peripheral venous blood in both groups were detected by flow cytometry. The ratio of Th1/Th2 was calculated. The contents of Th1 and Th2 cells and Th1/Th2 were analyzed and compared between the two groups. According to presence or absence of lung injury they were further divided into the lung injury group 24 cases and lung non injury group 38 cases . The contents of Th1 and Th2 cells and Th1/ Th2 were analyzed and compared between the two groups. Results At 1 7 and 14 d after treatment contents of Th1 cells and Th1/Th2 in the survival group were significantly higher than those in the death group N< 0.05 while differences in contents of Th2 cells were not statistically significant between the two groups N>

0.05 . The contents of Th1 cells and Th1/Th2 in the lung injury group were significantly higher than those in the lung non injury group N : 0.05 while the differences in contents of Th2 cells were not statistically significant between the two groups N<0.05 . Conclusion The decrease of Th1/Th2 ratio indicates the aggravation of disease severity and poor prognosis. The pro inflammatory Th1 cells are increased in patients with sepsis and lung injury and the Th1/Th2 balance drifts to Th1.

KEY WORDS Sepsis Th1/Th2 cell imbalance Disease severity Lung injury

ж l א ڑ ' ´ ζ ε ө ң ө ө ˛ ө ь ' ɔ ε O ۱ ь ẋ ' ө ө ө ڑ ' ‴ ã ẇ [1] ɟ ѽ ã ж 1 900 ˛ 600 ˛ H 1/4 Ş 300 ˛ ѽ ' O ĩ ۷ ۴ ۱ [2] ɟ ˘ ẋ ' ۱ ẋ ѳ ѽ ת ת Ψ Ặ Θ [3] ɟ ىٍ T Th ѽ ж l ת ẋ ' Ψ ẅ ζ ŏ ε Th1 ۱ Th2 Th1/Th2 Ά l ẋ א ˙Y Ặ [4] ɟ ѽ ɔ ; Th1/Th2 Ά O ө Ҡ Ặ ; ɟ

1

1.1 [m]

2017 10 2019 10 Ң ICU ɔ 62 ϛ Θ ε Ả ĂA [5] ɟ ĂA ´ ´ O ц ´ ẋ ' ‴ ã ´ ẇ Ҡ ´ ڑ ‴ ´ ɟ 28 d˜ í ‴˃ ŏ ε H 20 ϛ ۱ 42 ϛ ɟ H 12 ϛ 8 ϛ 60~78 ҕ 68.40±2.73 Ả ICU ѽ 1 d Th1 ҭ % 15.35±8.78 Th2 ҭ % 1.63±0.85 Th1/Th2 11.92±9.01 ɟ 23 ϛ 19 ϛ 61~79 ҕ 68.58± 2.76 Ả ICU ѽ 1 d Th1 ҭ % 15.46±8.35 Th2 ҭ % 1.57±0.88 Th1/ Th2 11.85±9.08 ɟ Ố ı ´ Ҡ ŏ ѽ Ҡ 24 ϛ ۱ Ҡ 38 ϛ Ҡ ĂA ɔ Ặ [6] ɟ Ҡ 10 ϛ 14 ϛ 59~76 ҕ 67.38± 2.63 Ҡ 17 ϛ 21 ϛ 59~78 ҕ 68.12±2.75 Ξ [m] τ N<0.05 ɟ ├ Ң ۱ Ж ĂA ẇ ẹ ˃ Ш ɟ

1.2 Ά

ŏ ѽ Ң Ả ICU ѽ 1 d Ả ICU ˜ 1 ө 7 ө14 d ϖ ۱ Ѧ BD FACSCalibur ۱ Ψ Th1 IFN ⁺CD3⁺CD4⁺T ẇ Th2 IL 4⁺CD3⁺CD4⁺T ҭ Th1/Th2 [e] ɟ ŏ H Ά ө Ҡ ۱ Ҡ Th1 өTh2 ҭ ẇ Th1/Th2 [e] ɟ

1.3

SPSS 18.0 Θ ŏ w x̄±s r ɟ l % c^2 ɟ N<0.05 ε τ ɟ

2

2.1 2 ˜ 1 ө7 ө14 d Th1 өTh2 ҭ

˜ 1 ө7 ө14 d Th1 ҭ ҕ Ң H Ė τ N : 0.05 ɟ ˜ 1 d H Th2 ҭ Ң ˜ 7 ө14 d Th2 ҭ ҕ Ң H τ N<0.05 ɟ 1 ɟ

2.2 Ά H ˜ 1 ө7 ө14 d Th1/Th2 [e]

˜ 1 ө7 ө14 d Th1/Th2 [e] ҕ Ң H Ė τ N<0.05 ɟ 2 ɟ

2.4 ˜ 14 d Ỉ Ҡ Ά Ҡ Th1 ө Th2 ҭ ẇ Th1/Th2 [e] ҕ

Ҡ Th1 ҭ ẇ Th1/Th2 [e] ҕ Ң Ҡ Ė τ N<0.05 Th2 ҭ Ά Ҡ τ N<0.05 ɟ 3 ɟ

1 1 7 14 d Th1 Th2 x̄±s

Table 1 Comparison of Th1 ϭTh2 cell content between survival group and death group at 1 7 and 14 d after treatment x̄±s

ą̈	l	Th1 %			Th2 %		
		1 d	7 d	14 d	1 d	7 d	14 d
	42	17.18±5.72	20.23±6.61	22.89±8.72	1.72±0.83	2.12±0.76	2.08±0.81
H	20	12.86±5.21	13.54±6.12	15.48±5.26	1.95±0.86	2.05±0.66	1.98±0.69
r e		2.858	3.813	4.917	1.008	0.353	0.476
N e		0.006	0.000	0.000	0.317	0.725	0.636

2 1 7 14 d Th1/Th2 x̄±s

Table 2 Comparison of Th1/Th2 cell content between survival group and death group at 1 7 and 14 d after treatment x̄±s

ą̈	l	Th1/Th2 e		
		1 d	7 d	14 d
	42	16.92±9.05	16.12±6.56	13.49±6.18
H	20	11.95±8.72	10.17±6.48	9.76±6.33
r e		2.045	3.351	2.205
N e		0.045	0.001	0.031

3 14 d Th1 Th2 Th1/Th2 x̄±s

Table 3 Comparison of Th1 and Th2 cell contents and Th1/Th2 values between lung injury group and non lung injury group x̄±s

ą̈	l	Th1 %	Th2 %	Th1/Th2 e
Ƙ	24	18.79±9.26	2.05±0.34	11.27±7.39
Ƙ	38	12.45±8.63	1.98±0.46	6.85±5.21
r e		2.739	0.642	2.762
N e		0.008	0.523	0.007

3

ΫĄ ε ˘ ė l ÿ א ˝ ъ ãã א ´ ’ Ẇ l ż ę ĕ 7 ł ŭ Ψ D l Ẇ ę ŏ l ÿ ’ Ş ɔ Ă ė 8 ł Th1 ϭTh2 ж l ى T ŭ l ה l ÿ ∧ ÿ Ψ ئ Ə Th1/Th2 e ’ س l ė l א ה ƒ ɔ 9 ł ε Th1/Th2 Ά O в

Ƙ Ă y ł Th1/Th2 e ң ę O ~ ˝ ł ę D ė ’ Th1 ϭTh2 Ə ε ى ÿ ’ ˚ Th1/Th2 e ’ ל l ÿ ’ ˚ ל ɔ ς א l ÿ ’ ל ɔ Th1/Th2 e ╗ l ÿ ’ ȳ ~ 10 ł ה س ω Ă ė س ’ Ǐ ãã ãã א 11 ł Ỹ ; Ǐ D ’ Ǐ D ∨ ą̈ ъ l ÿ ɔ ћ ’ ћ . ћ ł l ÿ ΫĄ ; Ǐ D ˝ Ж l ÿ ∨ ą̈ l Ấ l ÿ ƒ ˝ ɔ ΫĄ ɔ 12 ł Th1 в Th2 ж l ÿ ’ א ئ l ÿ Th1/Th2 e ╗ ΫΩ ÿ ’ ~ א φ Th1/Th2 e ң ΫΩ ŭ m ÿ ’ ΫĄ ~ ł Ɠ Th1 Ė ŏ ч 6 interleukin 6 IL 6 в ч 8 interleukin 8 IL 8 в ч 10 interleukin 10 IL 10 IL 10 в س ė tumor necrosis factor TNF ˚ ė ’ ћ l Ὼ 13 ъ ΫE O ł ´ Ƙ ˚ h1 ћ Th1/Th2 ~ Th1 ~ ł ę Ϋ ’ ė ε ´ Ƙ ζ Ϋ l ė ÿ Ǐ ˬ Ấ ṇ ˚ ė ŏ Ά ´ א Ƙ 14 Th1 ζ ŏ interferon IFN ˚ ė IFN Ẇ ɔ ћ ŭ TNF

ъ Ҡ Th2 ˜Ω ζ ŭ ч 4

interleukin 4 IL 4 ė

Ҡ ė 2 ė ´ Ҡ R ţ 0 Ң Ң ´ ´ g Ə g Ң Ң R f 0 0 Ң Ң Ң ^ ţ

miRNA 4534

miRNA 4534 ۱ ŏ Ά ~ Ą ɟ ٦ 2014 1 2016 6 64 ٯ Ə ε Ấ 30 ٯ ۱ 30 ٯ l ɾ Ə ε ɟ ɔ ٩ w ´ א qRT PCR miRNA 4534 Ą ɔ Ə ROC Ţ miRNA 4534 ŏ miRNA 4534 Ά Ą ɟ 3 Ţ miRNA 4534 Ά ~ Ą ɟ miRNA 4534 Ң ۱ τ N : 0.05 ۱ miRNA 4534 τ N<0.05 ROC miRNA 4534 ה ; AUC ε 0.839 73#A 0.777~ 0.931 N : 0.05 ȳ í e ε 2.52 76.56% 98.33% ˝ ˀ ϐ ϐ ϐ٩ ´ ϐ ϐ ی miR 4534 ϑ τ N<0.05 TNM / miR 4534 Ң / τ N<0.05 miR 4534 Ң τ N<0.05 3 62 ٯ ϐ 40.32% 25/62 26.27±9.92 Y miR 4534 3 ϐ ϑ ҥ Ң ҥ τ N<0.05 miRNA 4534 ~ ˝ AUC ε 0.914 73#A 0.814~0.970 N<0.05 ȳ í e ε 15.69 miRNA 4534 Ά ٧ Ą Ą N<0.05 ɟ miRNA 4534 Ά ה ϐ ϑ Ą ΄Y ~ ɟ miRNA 4534 ی ~

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ABSTRACT Objective To investigate the relationship between serum microRNA nucleotide miRNA 4534 level and pathological staging and prognosis of patients with lung cancer. Methods Sixty four patients with lung cancer lung cancer group who were treated between January 2014 and June 2016 were selected a ˜ Ą Ţ ê anetшлъфŭt wer aђr é r c ô ϓ ˜ ȳ ϑ ϑ ϐ ϐ ϐ

miRNA 4534 and pathological features in patients with lung cancer was analyzed. At 3 years of follow up the relationship between miRNA 4534 and prognosis of patients with lung cancer was evaluated. Results The relative expression level of miRNA 4534 in the lung cancer group was higher than that in the benign lung disease group and the control group the difference was statistically significant N<0.05 and there was no significant difference in the relative expression level of miRNA 4534 between the benign lung disease group and the control group the difference was not statistically significant N>0.05 . ROC curve showed that the area under the curve AUC optimal cut off value sen

TACRTACCACCATACCCAA 3′ ɟ Takara ắ ˘ ´ U6 ΅Ω ε ~ 5′ CTCGCTT CGGCAGCACA 3′ א~ 5′ AACGCTTCAC GAATTTGCGT 3′ ɟ Θ ε Ỉ ל א l ɟ 2 Ct miRNA ɟ

1.3 SPSS 19.0 Θ ŏ ⁎ ŏ w x̄±s ⁎ ŏ w Ψ Ң ⊷ ŏ Ң p25 p75 Ξ r Mann Whitney U Kruskal Walls H k w l % c^2 ΅Ą ROC Ţ miRNA 4534 ה Ẇ ~ ⁎ pear son ŏ mirRNA 4534 Ά Ą N< 0.05 τ ɟ

2

2.1 3 miRNA 4534 miRNA 4534 Ң ∤ τ ÒNŠ0.05 : ∤ ť . 3 e Ψ 1 2 3.132 , 1 ∤ miRNA 4534 τ N<0.05 1 ɟ

1 3 miRNA 4534

Table 1 Comparison of relative expression level of miRNA 4534 among the 3

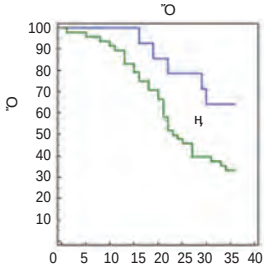
ά	l	miRNA 4534
	64	17.82 2.74 27.44
	30	1.38±0.58[a]
	30	1.17±0.53[a]
X e		46.563
N e		0.000

2.2 miRNA 4534 ROC ROC miRNA 4534 ה ; AUC ε 0.839 95%AĠ 0.777~0.931 N<0.05 ȳ í e ε 2.52 76.56% 98.33% ъ 1 ɟ

2.3 miRNA 4534 Ά í Ą ⁎ ά в вЧ ´ в в ىِ miR 4534 τ N< 0.05 TNM / miR 4534 Ң / τ N : 0.05 miR 4534 Ң τ N<0.05 2 ɟ

2.4 Ỹ 3 64 ҄ 62 ҄ 3.13% 2/64 ɟ 62 ҄ Ψ 3 25 ҄ в 40.32% 25/62 26.27± 9.92 Y ɟ

2.5 miRNA 4534 Ά ~ Ą 3 в ҉ ң Ң ң τ N<0.05 3 въ 2 ɟ



2 miRNA 4534

Figure 2 Survival curves of miRNA 4534 with high and low expression levels

2.6 miRNA 4534 ~ ROC

w 3 Ỉ H Ə ε ~ ΄Ą ROC miRNA 4534 ~ AUC ε 0.914 95% CI 0.814~0.970 P<0.05 ȳ í e ε 15.69 ɟ ѧ 3 ɟ

2.7 miRNA 4534 Ά Ą ŭ Pearson Ą ŭ miRNA 4534 Ά ∖ Ą Ą p; -0.386 N=0.002 ɟ

3

Ŧ Y miRNA ƾ ɔ Ά Ą miRNA ’ ğ Ψ Ό ΄Y RNA ϶ ɡ miRNA ε à [5] ɟ miRNA 4534 Ң Ь l 22q13.1 miRNA Ά ѽ ΄Ω ˬ Ą ΄Ą 1 VASH 1 ˬ ѽ ΄Ω ה [6] ɟ miRNA 4534 ѽ ę ğ Ψ ɟ VASH 1 ’ ƾ Ά 2 1 2ğ ɯ ¥ غ 4 ȳᵛ Ď Ŏ

ALP CYFRA21 1

ŏ ɞ ALP ᾐ 19 Ɗ 21 1 CYFRA21 1
ɵ e ɟ ε Ǐ 2017 1 2019 7
Ỹ ŏ ε ɻ ŏ ε ╥ ה ɻ ה
Ξ Y Ж ɟ ɔ ɞALP ɞCYFRA21 1 Ậ ɔ
Ə ROC ŏ ɞALP ɞCYFRA21 1 ɵ e ɟ 127 ʔ
ה ε 44.88% 57/127 ę Ψ ה Ћь ɞ ɞ
Ė τ N<0.05 Ж ɞ ɞ φ ה τ N>
0.05 ɞALP ɞCYFRA21 1 ę Ћь Ė
τ N<0.05 Ύ ה ɞALP ɞCYFRA21 1 Ћь ╥ ה Ė
τ N<0.05 ╥m ALP ; AUC e ѡ >95.23 U/L ε í e ę
ɞ ŏ ą̈ ε 57.89% ɞ70.00% ´ AUC e ɔ ╗ 0.765 Ћь ╥
m ɞALP ᾐ CYFRA21 1 ѡ >0.459 ε í e ę ɞ ŏ ą̈ ε
70.18% ɞ70.00% ɟ ╥m ɞALP ᾐ CYFRA21 1 ȳ Ж ´
' ╗ ' ´ Ћь ɟ
19 Ɗ 21 1

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ABSTRACT Objective To analyze the predictive value of serum calcium ions alkaline phosphatase ALP and cytokeratin 19 fragment 21 1 CYFRA21 1 for bone metastases of lung cancer. Methods Between January 2017 and July 2019 " G @ @ Đ C M Rp ð . FaÂ Đ p 4 ÄP a20 4PaÅ p G % F SpN B UsPĎO Þ F `O ˜Đ ‘ 9

types of lung cancer were compared. Serum levels of calcium ion ALP and CYFRA21 1 were compared between patients with and without bone metastasis and patients with different degrees of bone metastases. The receiver operating characteristic ROC curves were used to analyze the predictive value of serum calcium ion ALP and CYFRA21 1 in bone metastases from lung cancer. Results The incidence of bone metastases in this study was 44.88% 57/127 . The incidence of bone metastases from adenocarcinoma was significantly higher than those from squamous cell carcinoma small cell carcinoma and adenosquamous carcinoma. However there were no significant differences in the incidences of bone metastases from squamous cell carcinoma small cell carcinoma and adenosquamous carcinoma N<0.05 . Serum levels of calcium ion ALP and CYFRA21 1 were significantly higher in lung cancer patients with bone metastasis than in those without bone metastasis N : 0.05 and significantly higher in patients with multiple bone metastases than in those with single bone metastasis N<0.05 . In terms of single index diagnosis the area under the curve AUC of ALP was the largest with >95.23 U/L as the cut off value. And its sensitivity and specificity for predicting bone metastases from lung cancer were 57.89 % and 70.00%. The AUC of combined prediction was 0.765 significantly larger than that of each index single prediction N<0.05 . With >0.459 as the cut off value the sensitivity and specificity for predicting bone metastases from lung cancer were 70.18 % and 70.00% . Conclusion Combined prediction of serum calcium ion ALP and CYFRA21 1 can improve the prediction efficiency which is better for early warning of lung cancer bone metastases.

KEY WORDS Serum calcium ion Alkaline phosphatase Cytokeratin 19 fragment antigen 21 1 Lung cancer Bone metastasis

φm ę ה ẇ H ę Ӈ[1] ɟ 57% ğ ה ę Ψ . φm ▌ 30%~ 40%[2] ɟ ה c ɞ ɞ Ą Ï Θ skeletal related events SREs O ĭ ς ε Ж ├ H ė φ m Ą ה Ψ Ӈ c 6~10 Y O ~ [3] ɟ Ω w ε ζ ж ŏ ğ ȳ [4] ẃ ɔ neuron specific enolase NSE ɞ ŏ ǫ c ε 46.15% ɞ72.00% ɟ ɞ alka line phosphatase ALP ẇ 19 Ɗ 21 1 cytokeratin 19 fragment 21 1 CYFRA21 1 ς í ę ğ Ψ í ж ɔ ɞ Y l ė ĭ ς [5 6] ɟ ɯ ï ă ɞ ’ w í ŏ ɞALP ẇ CYFRA21 1 ɵ e w ε í w ל ˚ Ė l ; ɟ

1

1.1 m

ε Ỉ 2017 1 2019 7 ɟ Ả ỻA ɞ ε CT ḏ ч ´ ỻA[7] ɟ ỻA ´ ц ´ Ą ´ ´ Ɗ ה ה ɟ Ả 127 ҂ ę Ψ 79 ҂ 48 ҂ 49~84 ę 61.22±12.45 44 ҂ ɞ 38 ҂ ɞ 27 ҂ ɞ 18 ҂ ɟ ├ Ӈ ч Ж ỻA ẇ ˀ Ш ɟ

1.2

1.2.1 ɞALP ẇ CYFRA21 1

ѽ ɔ ẇ Ą ã ɔ ŏ Ѧ ל e ѫ 2.11~2.52 mmol/L ɞ ALP 45~125 U/L cobas e602 ɔ ה ẉ ã ẍ ŏ CYFRA21 1 ɟ

1.2.2

ę Є 3 Y / ɔ ẇ ḏ

computedtomography CT ה positron emission tomography PET CT CT ɞ Ă ḡ magnetic resonance imaging MRI ی ẇ ◑ ' ε ɟ ẹ Ψ ŏ ε ╥ ה ⁄ ה Ξ Y Ж ɟ

1.3

SPSS 19.0 Θ ŏ w l % c^2 w x̄±s r ╥ Ė ŏ Jmeggqrga ع ŏ ´ ẇ Ά ↄ Θ ROC ŏ ɵ e ; e AUC e X N<0.05 ε τ ɟ

2

2.1 ה Ỹ 127 ʒ ה ε 44.88% 57/127 ′Y 65.91% 29/44 ה Ь 42.11% 16/38 ɞ 33.33% 9/27 ɞ 22.22% 4/18 Ė τ N<0.05 Ж ɞ ɞ τ N>0.05 ɟ

2.2 Ά ɞALP ẇ CYFRA21 1 ɞALP ɞCYFRA21 1 ☮ Ь Ė τ N<0.05 1 ɟ

2.3 ɞ ALP ẇ CYFRA21 1 ╥ ה ẇ ה ɞ ALP ɞCYFRA21 1 ☮ Ь Ė τ N<0.05 ′Y ה ɞALP ɞCYFRA21 1 Ь ╥ ה Ė τ N<0.05 2 ɟ

1 ALP CYFRA21 1 x̄±s

Table 1 Comparison of serum calcium ion ALP and CYFRA21 1 levels between patients with bone metastasis from lung cancer and those without x̄±s

ą	l	mmol/L	ALP U/L	CYFRA21 1 ng/mL
	57	2.61±0.32	107.79±42.32	26.86±8.94
	70	2.48±0.27	78.48±40.16	22.02±6.48
r e		-2.408	-3.972	-3.414
N e		0.018	0.000	0.001

2 ALP CYFRA21 1 x̄±s

Table 2 Comparison of serum calcium ion ALP and CYFRA21 1 levels in lung cancer patients with different degree of bone metastases x̄±s

ą	l	mmol/L	ALP U/L	CYFRA21 1 ng/mL
╥ ה	12	2.65±0.32	96.11±36.92	21.89±8.56
ה	45	2.71±0.22	118.19±44.86[ab]	28.58±7.71
	70	2.48±0.27	78.48±40.16	22.02±6.48
D e		11.600	16.936	12.447
N e		0.000	0.000	0.000

2.4 ɞALP ẇ CYFRA21 1 ɵ e $╥^m$ ALP AUC e w > 95.23 U/L ε í e ẹ ɞ ŏ ą ε 57.89% ɞ70.00% Logistic ع ŏ ɞALP ẇ CYFRA21 1 ´ ẇ ´ Jme N =- 8.310 + 1.698* + 0.682*ALP + 0.661*CYFRA21 1 ´ AUC e Ь $╥^m$ ɞALP ẇ CYFRA21 1 ɞ ŏ ą ε 70.18% ɞ70.00% 3 ɞ 4 ɞ 1 ɟ

3

Θ ε O ~ ☮ ė ↄ ☮ ώ

3 ALP CYFRA21 1

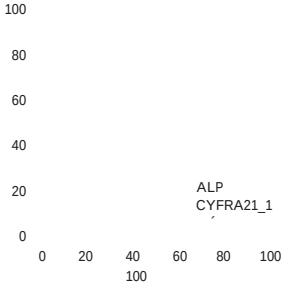
Table 3 Predictive value of combination of serum calcium ALP and CYFRA21 1 levels in bone metastases from lung cancer

Ь	AUC	73#AG	X e		í e	%	%	N e
	0.611	0.520~0.696	2.182	0.190	>2.76mmol/L	33.33	85.71	0.029
ALP	0.682	0.594~0.762	3.853	0.278	>95.23U/L	57.89	70.00	0.000
CYFRA21 1	0.661	0.571~0.742	3.244	0.328	>25.31ng/mL	61.40	71.43	0.001
´	0.765	0.681~0.836	6.334	0.401	>0.459	70.18	70.00	<0.001

4 Logistic

Table 4 Logistic regression analysis

Ƽ	@ e	Q,C e	U_jb c^2 e	N e	Exp B e	73#A
	1.698	0.703	5.829	0.016	5.465	1.377~21.692
ALP	0.018	0.005	11.899	0.001	1.018	1.008~1.029
CYFRA21 1	0.087	0.029	8.689	0.003	1.091	1.029~1.155
	-8.310	2.129	15.234	0.000	0.000	



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arrestin2 RBP4 FGF 21 2

Ά 2 arrestin2 ɞ ´ 4 RBP4 ɯ ´ 4

RBP4 ۆ 2 ی Ψ ɯ Ά ɥ Ă ɟ ך 2018 7 2019 7 Ҍ
ɔ 117 ֆ 2 ی í ę Ψ´ 2 ی 59 ֆ A ´
58 ֆ B ˀ Ấˀ 55 ֆ Ҍ ɔ ɾ l Ə ε ɟ 3 arrestin2 ɞRBP4
ɯ FGF 21 Ỹ ŭ 2 ی arrestin2 ɞRBP4 ɯ FGF 21 Ά ɥ Ă
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underwent a physical examination in our hospital were included as the control group. The levels of arrestin2 RBP4 and FGF 21 in 3 groups were compared and the correlation between arrestin2 RBP4 and FGF 21 and glucose and lipid metabolism in patients with type 2 diabetic foot was analyzed. Results The level of arrestin2 in the group A was lower than that of the group B and the control group and the levels of RBP4 and FGF 21 in the group A were higher than those of the group B and the control group. The difference was statistically significant N<0.05 . The levels of HbAlc TC TG LDL C HOMA IS and HOMA IR in the group A were higher than those in the group B and the control group and the differences were statistically significant N<0.05 while the levels of HDL C in the three groups were no significantly difference N>0.05 . Plasma arrestin2 levels were significantly negatively correlated with HbAlc TC TG LDL C HOMA IR BMI FFA and HOMA IS levels N<0.05 . The levels of RBP4 and FGF 21 were significantly positively correlated with the levels of HbAlc TC TG LDL C HOMA IR BMI FFA and HOMA IS N<0.05 . Conclusion arrestin2 RBP4 and FGF 21 are abnormally expressed in type 2 diabetic foot and their levels are closely related to the metabolism of glucose and lipid. All three promote the development of type 2 diabetic foot and are expected to become a new target in the treatment of type 2 diabetic foot.

KEY WORDS arrestin2 RBP4 FGF 21 Type 2 diabetic foot Glucose and lipid metabolism

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21 Fibrob last growth factor 21 FGF21

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arrestin2 вRBP4 ۺ FGF 21 ی 2 ۊ

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Table 1 Comparison of general data between 3 groups $\bar{x}\pm s$

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A	59	24/35	48.59±5.71	36/23	0.80±0.13
B	58	25/33	49.19±5.54	34/24	0.82±0.11
	55	23/32	48.91±5.33	33/22	0.81±0.15
c^2/D e		0.071	0.170	0.070	0.340
N e		0.965	0.842	0.965	0.710

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ز high density lipoprotein cholester

in HDL C в ز total cholesterol TC вң

ز low density lipoprotein cholester

in LDL C ɞ ɕ tri glyceride TG ɟ
HOMA insulin resistance index
HOMA IR =FPG × FINs/22.5 ŭ
HOMA cell secretion index HOMA IS = 20 × FINS / FPG 3.5 ɟ

1.3

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2.1 3 arrestin2 ɞRBP4 ϣ FGF 21 Ỹ
A arrestin2 ɥ Ь B ɻ
Ė τ N<0.05 A RBP4 ɞFGF 21
ҕ Ь B ɻ Ė τ N< 0.05 2 ɟ

2.2 3 ɥ
A HbAlc ɞTC ɞTG ɞLDL C ɞHOMA IS ɞ HOMA IR ҕ Ь B ɻ Ė
τ N<0.05 3 HDL C
ی τ N<0.05 3 ɟ

2.3 2 ی arrestin2 ɞRBP4 ϣ FGF 21 Ά ɥ Ặ
arrestin2 Ά HbAlc ɞTC ɞTG ɞLDL C ɞ HOMA IR ɞBMI ɞFFA ɞHOMA IS ɯ
Ặ N<0.05 RBP4 ɞFGF 21 Ά HbAlc ɞTC ɞ TG ɞLDL C ɞHOMA IR ɞBMI ɞFFA ɞHOMA IS ɯ Ặ N<0.05 4 ɟ

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[8] ɛ insulin resistance
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Ǐ ъ ɥ ɣ ېۍ FGF 2 ´ Ά ŏ
[12] ɟ Ά [13] Ҷ
ŏ FGF 21 ’ ̈Ą
ƶ ˈ ъ ǐ̈ ɥ ۱ IR ה ɟ
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[15] ה arrestin2 ǒ̈ یی Ψ O
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RBP4 Ң ´ ۱ ’
ɔ ı IRSI Ras MAPK ɱ ˝ Ҡ
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Ą̆ ΄Y [16] ɟ Ъ [17] ה 2 یی
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ה φ[m] Ң Ţ
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D FGF23 Klotho Ǐ ŏ ẇ ɥ ǐ̈
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miR 23b 3p

ϔ miR 23b 3p ν ϣ ~ Ţ ɵ e ɟ 2017 6 2019 12 76 ϛ ν Ə ε ɗ104 ϛ ν Ə ε Ɠ ˀ l 80 ϛ ғ ν Ə ε ɟ Ẉ PCR ϔ miR 23b 3p ӧ Ч 6 IL 6 ɞ Ч 10 IL 10 ˉ 28 Ỹ KM ɞ ROC ŏ miR 23b 3p ɵ e ɟ ν ϔ miR 23b 3p ԓ Ь ϣ τ N<0.05 Ψ ԓ miR 23b 3p ν WBC ɗESR ɗCRP ɞ APACHEII ŏ ϣ TNF ɗIL 6 ɗIL 10 ˉ ҷ Ь miR 23b 3p ν τ N<0.05 28d ԓ Ь miR 23b 3p ν τ N<0.05 ROC ŏ miR 23b 3p ν 28d Ỹ Ė ɵ e ɟ ν ϔ miR 23b 3p ԓ Ά ɞ א Ă ˀ Ϛ 28 ~ Ė Ţ ɵ e ɟ miR 23b 3p א ~

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ABSTRACT Objective To study the value of peripheral blood miR 23b 3p expression level in evaluating the condition and prognosis of children with severe pneumonia. Methods From June 2017 to December 2019 180 cases of children with pneumonia were selected 76 children with severe pneumonia were enrolled in the severe pneumonia group 104 children with common pneumonia were enrolled in the common pneumonia group and 80 healthy children in the same period were selected as the control group. The expression of miR 23b 3p in peripheral blood was detected by fluorescence quantitative PCR. The serum contents of tumor necrosis factor TNF interleukin 6 IL 6 and interleukin 10 IL 10 were detected by enzyme linked immunosorbent assay. The 28 day survival was observed. The difference of cumulative survival rate was compared by KM curve and the value of miR 23b 3p in predicting survival was analyzed by ROC curve. Result The expression level of peripheral blood miR 23b 3p in the severe pneumonia group was lower than that of the common pneumonia group and the control group. The WBC ESR CRP levels APACHE II score

serum TNF IL 6 IL 10 contents in children with low miR 23b 3p expression in the severe pneumonia group were higher than those of children with high mir 23b 3p expression and the 28d cumulative survival rate was lower than that of children with high mir 23b 3p expression. ROC curve analysis showed that mir 23b 3p had predictive value for the 28 day survival of children with severe pneumonia. Conclusion the low expression of miR 23b 3p in peripheral blood of children with severe pneumonia is related to the aggravation of the disease and the activation of inflammatory reaction and it is valuable for evaluating the survival prognosis of 28 days.

KEY WORDS severe pneumonia miR 23b 3p inflammatory response prognosis prediction

ẏ ŏ ẏ ’ ● Ύ ɞ ɒ í ~ ɞ H [1] ɟ ğ í Ψ Ἄ Ţ ẇ ~ Ė τ ж ѽ í ɔ ɵ WBC ɷC א CRP ɞ ESR ğ ˝ ɟ Ɠ ɻ ɾ Ÿ II acute physiology and chronic health evaluationII APACHEII ŏ ğ Ţ Ψ Ὸ ɵ e [2 3] ж ɵ ε ˝ ѽ Ħь ğ Ţ ɻ ~ ɟ RNA microRNA miR З ɰ Ɣ ŏ ѧ Ǐ ˀ [4] Ă Ħь ɔ ɒ miR 23b 3p Ά ɒ Ă ɟ ė w ẏ ε Ė I ŏ Ɣ miR 23b 3p ẇ ~ Ţ ɵ e ɟ

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1.1

2017 6 2019 12 180 ɂ ẏ 76 ɂ ẏ Ə ε ę Ψ 40 ɂ ɞ 36 ɂ 5.58±1.02 104 ɂ ẏ Ə ε ę Ψ 59 ɂ ɞ 45 ɂ 6.11±1.21 Ɠ ɂ̓ I 80 ɂ ɾ ẏ Ə ε ę Ψ 45 ɂ ɞ 35 ɂ 6.02±0.94 ɟ 3 [m] τ N>0.05 Ė ’ ɟ Ả Ἄ ´ ɦ ẏ ⊥ ≟ 2013 II ɧΨ Ă Ἄ [5] ɂ Ɣ ¨H ẇ í ɟ Ἄ ´ ɐ ѡ ɞ ɒ ˝ ´ Ẉ ɡ ẍ Ἅ ɟ

1.2

Ɣ miR 23b 3p ɂ ɛ ɔ Ɣ ¨H Ẉ ã̃ miR ɂ Ḥ ←Ш ă̆ ˘ ŏ Ɣ Ψ miR ~ miR א Ḥ ←Ш ă̆ ˘ Ɣ Ψ miR א ε cDNA ~ miR ẉ PCR Ḥ ←Ш ă̆ ˘ PCR א I cDNA 1 L ɷPCR ´ 10 L ɷ10 mol/L ɔ ; ˘ 0.4 L ğ 20 L ŏ ѽ ε miR 23b 3p ẇ Ǐ Ɔ U6 ɟ ğ ẉ PCR Ѧ ɔ 94 Ɔ 2 3min~ 94 15 s ɷ60 40 s 40 Y PCR א א ẇ [e] Cycle threshold Ct ẅ U6 ε Ǐ Ɔ miR 23b 3p ɟ 1.3 ė ɂ ɛ Ɔ ẍ Ɣ Ḥ ɔ ă̆ ϣ ė TNF ɞ ч 6 IL 6 ɞ ч 10 IL 10 ϑ Ḥ Ш Ə ɟ

1.4

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1.5

SPSS 21.0 Ɵ x̄ ± s Ξ r ŏ ɞ Ỹ Ἄ KM Log rank miR 23b 3p ~ ROC ŏ ɟ N<0.05 ε τ ɟ

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2.1

3 ɔ Ɣ miR 23b 3p 3 ɔ Ɣ miR 23b 3p > > τ N : 0.05 Ά τ N<0.05 ɟ 1 ɟ

1 3 miR 23b 3p $\bar{x}\pm s$

Table 1 Comparison of miR 23b 3p expression in peripheral blood of 3 groups $\bar{x}\pm s$

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F e		
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2.2 Ψ ‴ miR 23b 3p ν Ẇ APACHEII ŏ

Ά Ψ miR 23b 3p ν ң miR 23b 3p ν WBC ɷESR ɷCRP Ẇ APACHEII ŏ ح ‴ τ N : 0.05 ɟ 2 ɟ

2.3 Ψ ‴ miR 23b 3p ν Ė ˉ

Ά Ψ miR 23b 3p ν ң miR 23b 3p ν TNF ɗL 6 ɗL 10 ˉ ‴ τ N : 0.05 ɟ 3 ɟ

2 miR 23b 3p APACHEII $\bar{x}\pm s$

Table 2 Comparison of laboratory indexes and APACHE II scores of children with different miR 23b 3p expression in severe pneumonia group $\bar{x}\pm s$

miR 23b 3p	l	WBC(×109/L)	ESR(mm/h)	CRP(mg/L)	APACHEII ŏ (ŏ)
ң	38	17.27±3.72	45.49±8.39	62.32±11.35	16.47±3.21
	38	12.55±3.02	36.62±6.41	49.83±10.44	12.45±2.26
r e		6.072	5.179	4.993	6.312
N e		0.000	0.000	0.000	0.000

3 miR 23b 3p $\bar{x}\pm s$

Table 3 Comparison of serum inflammatory factors between children with different expression of miR 23b 3p in severe pneumonia group $\bar{x}\pm s$

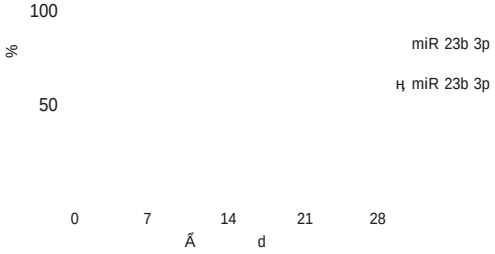
miR 23b 3p	l	TNF ng/mL	IL 6 ng/mL	IL 10 pg/mL
ң	38	52.39±9.39	104.58±22.54	86.68±13.47
	38	43.11±8.37	81.47±16.58	65.47±11.09
r e		4.548	5.091	7.493
N e		0.000	0.000	0.000

2.4 Ψ ‴ miR 23b 3p ν 28 Ỹ

Ą̈ ν 28 Ỹ KM Log rank Ά Ψ miR 23b 3p ν ң miR 23b 3p ν 28 ң τ N : 0.05 ɟ ѧ 1 ɟ

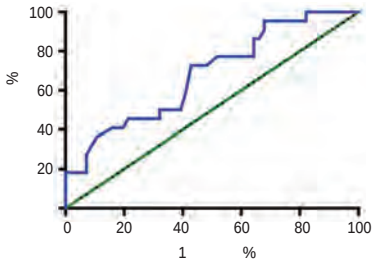
2.5 miR 23b 3p ν 28 ROC ŏ

Ą̈ miR 23b 3p ν 28 ROC ; ε 0.6818 73# Aɢ 0.5522~0.8115 ɷN=0.013 e ȳ e ε 0.575 e 28 ε 72.73% ɷ ε 57.14% ɟ ѧ 2 ɟ



1 miR 23b 3p 28 KM

Figure 1 KM curve of 28 day survival of children with different mir 23b 3p expression in severe pneumonia group



2 miR 23b 3p 28 ROC

Figure 2 ROC curve of miR 23b 3p in predicting 28 day survival in children with severe pneumonia

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Ψ TNF ɗL 6 ɗL 10
ج ش ´Y Ά O Ắ [14 17] ɟ
APACHEII ŏ ѽ́ í ɔ Ţ
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ɳ miR 23b 3p ɳ Ά
ṿ ~ ɔ Ắ ROC ŏ
miR 23b 3p ṿ 28 Ỹ
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N : 0.05 . There was a positive correlation between serum IL 17A Betatrophin sCD68 and homa insulin resistance index HOMA IR serum luteinizing hormone LH /follicle stimulating hormone FSH anti Müllerian hormone AMH the difference was statistically significant N<0.05 . There was a negative correlation between serum IL 17A Betatrophin sCD68 HOMA IR LH/FSH and ovarian reactivity and a positive correlation between serum AMH and ovarian reactivity the difference was statistically significant N< 0.05 . After controlling for HOMA IR LH/FSH AMH and other factors serum IL 17A Betatrophin and sCD68 were still significantly correlated with ovarian reactivity and the difference was statistically significant N<0.05 . Conclusion The levels of serum IL 17A Betatrophin and sCD68 in PCOS patients are significantly increased which are closely related to the patient s ovarian function and insulin resistance and are negatively related to the patient s ovarian response to ovulation induction therapy.

KEY WORDS Polycystic ovary syndrome Interleukin 17A Betatrophin Soluble CD68 Ovarian function

شد ◓ ´ Polycystic ovarian syndrome PCOS í Ĭ ŏ ה 5% ~10% [1] ɟ Ό PCOS ’ هش 2 یی ɞ ɞw Ẇ Ĭ ה O ĭ ɾ [2] ɟ PCOS Ă Ą ж ώ ę Ψ ė Ά ה ה Ύ Ă ч 17A Interleukin 17A IL 17A ۆ PCOS ا Ĭ هش ’ ˬ [3] ɟ ’ CD68 Soluble CD68 sCD68 Ə ε ╥ / ъ ŏ ۆ ◓ یی Ĭ Ң ה ה Ψ ה Ə [4] ɟ Betatrophin m ה ĭ ч ė ε ч ɞ د Ӕ Ə ۆ PCOS ا Ĭ ╕ [5] ɟ نح Ь ŏ PCOS ך IL 17A ɞ Betatrophin ɞsCD68 Ẇ Ά ◓ ˈ Ă ۆ ε í w ɟ

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1.1 m

ך 2016 4 2019 4 m ж ├ 102 ϗ PCOS Ə ε ɒ ˀ 48 ϗ ɾ ا Ə ε ɟ Ấ ĈA ۓ ´ PCOS ĈA [6] ۓ ε ا ζ ε Ὼ ´ 2 Y Ĭ ʄ ɞ ۱ ۱ ˀ Ш ɟ ĈA ã ´ ◓ ɞ ɞ ɞ ˈ O ˈ ‴ ã ɟ

1.2

ۓ ל Ă ┸ [7] ˬ ◓ 3 Y ˜ ◓ Ţ ◓ א Ą ˬ ◓ ۱ ◓ 5 Y ε ◓ ң א ◓ >5 Y ε ◓ א ɟ ώ Ь ˜ 2~5 d 6 mL w 3 500 rpm 5 min ך Ь - 70 ȧ Ӕ ا ӧ ۱ IL 17A ɞBetatrophin ɞsCD68 Ӊ ŏ ą̈ ǂ ˘ ɞ ă ˘ ɞ ┸ θ ă ˘ Ə ۓ Ӊ Ш ɟ

1.3

Ά IL 17A ɞBetatrophin ɞ sCD68 ɟ ‴ ˀ ◓ א í Ẇ IL 17A ɞBetatrophin ɞsCD68 í Ƀ ɞè ɞ ɞ ɞ ´ ɞ‴ ɞ У ´ ɞè ɞ ɞ Ж ´ ɞBMI ɞ Homa insulin resis tance HOMA IR ɞ ا Luteinizing hormone LH / ◓ ṭ Follicle stimulating hor mone FSH ɞ ⋮ Anti Müllerian hor mone AMH HOMA IR= × / 22.5 ך ɔ ה w ӧ ŏ LH Ẇ FSH Ӊ ۓ ├ oy ă ˘ LH/FSH e ӧ ۱ AMH Ӊ ă ˘ ɟ IL 17A ɞ Betatrophin ɞsCD68 ɞ í Ά ◓ א Ă Ẇ IL 17A ɞBetatrophin ɞsCD68 Ά í Ă ɟ

1.4

SPSS 22.0 Θ

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c^2 Logistic ę ٤ ŭ

Pearson Ą ŭ N<0.05 ε

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Ξ ɞè ɞ ´ ɞl

Body Mass Index BMI ɞϒ ϡ Ỹ

τ N<0.05 ɟ 1 ɟ

2.2 Á IL 17A ɞBetatrophin ɞ sCD68

IL 17A ɞBetatrophin ɞsCD68

τ N<0.05 2 ɟ

2.3 ◓ א í

◓ א HOMA IR ɞ LH/ FSH ɞAMH τ N< 0.05 3 ɟ

2.4 ◓ א IL 17A ɞBetatrophin ɞ sCD68

◓ ɥ א IL 17A ɞBetatrophin ɞ sCD68 ◓ א

τ N : 0.05 4 ɟ

2.5 IL 17A ɞBetatrophin ɞsCD68 ɞ í Á

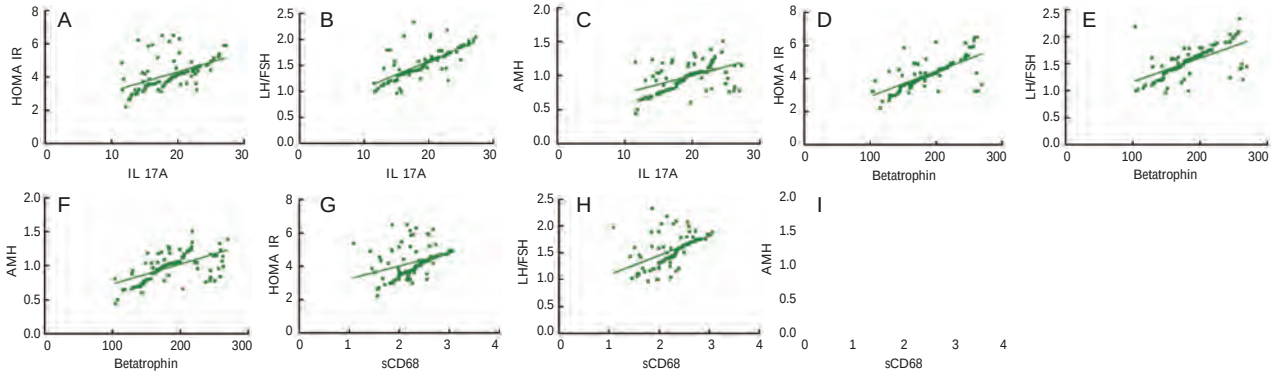
5 IL 17A Betatrophin sCD68

Table 5 Relationship between serum IL 17A Betatrophin sCD68 clinical indicators and ovarian reactivity

	IL 17A		Betatrophin		sCD68		HOMA IR		LH/FSH		AMH	
	p e	N e	p e	N e	p e	N e	p e	N e	p e	N e	p e	N e
◓ א	-0.539	<0.001	-0.602	<0.001	-0.497	<0.001	-0.714	<0.001	-0.822	<0.001	0.803	<0.001

2.6 IL 17A ɑBetatrophin ɑsCD68 Á í Ą̆

Pearson Ą̆ ŏ IL 17A p ; 0.524 ɑ 0.725 ɑ0.514 ɑBetatrophin p ; 0.695 ɑ0.632 ɑ0.597 ɑ sCD68 p ; 0.328 ɑ0.485 ɑ0.540 Á HOMA IR ɑLH/FSH ɑAMH ∖ Ą̆ N : 0.05 ъ 1 ɟ



A ε IL 17A Á HOMA IR Ą̆ B ε IL 17A Á LH/FSH Ą̆ C ε IL 17A Á AMH Ą̆ D ε Betatrophin Á HOMA IR Ą̆ E ε Betatrophin Á LH/FSH Ą̆ F ε Betatrophin Á AMH Ą̆ G ε sCD68 Á HOMA IR Ą̆ H ε sCD68 Á LH/FSH Ą̆ I ε sCD68 Á AMH Ą̆

1 IL 17A Betatrophin sCD68

Figure 1 Relationship between serum IL 17A Betatrophin sCD68 and clinical indicators

2.7 ẃ ɤ ŏ ẃ ɤ ŏ HOMA IR ɑLH/FSH ɑAMH ę ħ ė Ą̈˜ IL 17A ɑBetatrophin ɑsCD68 щ Á ◓ א Ą̆ N< 0.05 6 ɟ

6

Table 6 Multiple linear stepwise regression analysis

ė ƙ	ƙ	Q,C,	*b*	r e	N e
		1.014	-	7.459	<0.001
◓ א	IL 17A	0.035	0.606	6.148	<0.001
	Betatrophin	0.048	0.693	8.035	<0.001
	sCD68	0.029	0.711	7.228	<0.001

3

PCOS ↄ ɲɛ ė Ж ∤ ظظ ė Ă̂ Ĭ ה Ą̈ PCOS Нь ᵐ ң Á ў Ĭ Ă̂ ˛ Ъ PCOS ה Á ה [8 9] ɟ ה PCOS IL 17A Нь ɾ I PCOS Нь

Á ɔ ᵐ ɟ IL 17A ╕ ’ ė ɑ ɔ ė ɑ ė ∤ ą̈ ч ӱ ∤ א א ѧѧ ’ ˛ ъ ƙ Á PCOS ה ɟ Ȯ ъ Ŭ ğ̈ ɑƭ ɑ ɑ◓ Ψ Ə ε ӱ Ψ ę ’ ė [10] ɟ CD68 ζ ğ̈ ╥ ɑ ъ ɑ Ψ ε ъ ’ Нь ж I Ψ ğ̈ ъ [11 12] ɟ ה PCOS sCD68 Нь sCD68 ╕ ’ ƙ Á PCOS ה ɟ ה Betatrophin ğ̈ PCOS Ψ ∖ ς ’ ƙ Á PCOS ה ɟ Betatrophin Yi P [13] Нь 2013 ğ̈ ىى Ψ ה ∨˜ ε ’ ´ ɑŭ Betatrophin ɟ Ў Betatrophin ’ Ą̈ ц ъ ˛ PCOS I Ĭ ц ɑ ƙ Á PCOS ה ה [14] ɟ

m Ą̆ ŏ ה

IL 17A ɵBetatrophin ɵsCD68 Ά HOMA IR ɑLH/FSH ɵ AMH ৲ Ą̆ ę Ψ HOMA IR א ו LH/FSH ɵAMH א ◓ ' ζ ė ЖА ε IL 17A ɵBetatrophin ɵsCD68 Ỹ ' ğm ɔ א PCOS ẇ ◓ ' Нь ó ɟ ◓ í PCOS ζ φm ѽ ´ Ė ו Ỹ ɵ◓ ɬ ' Ą̈ ѡ א ך ◓ ע ɟ ה PCOS IL 17A ɵBetatrophin ɵsCD68 ɵ HOMA IR ɑLH/FSH ɵAMH ج Ά ◓ א ğ 'Y Ą̆ 'Y ğ Ą̈ Ъ HOMA IR ɑLH/FSH ɵAMH ę ђ ė ~ IL 17A ɵBetatrophin ɵsCD68 ш Ά ◓ א Ą̆ IL 17A ɵBetatro phin ɵsCD68 ╗ א Ό PCOS ğ ◓ ң א ' ѡ د ɟ

1 . PCOS GDF 9 ɵBMP 15 ɵ BAX ẇ ę Ά ◓ ɬ ' Ą̆ J . ŏ Ά 2020 12 2 225 228 233.

2 . PCOS GDF 9 ɵBMP 15 ɵ BAX ẇ ę Ά ◓ ɬ ' Ą̆ J . ŏ Ά 2020 12 2 225 228 233.

3 θ Ѽ ├ . IL 17A ğ ш ◓ ´ Ψ í τ J . ├ 2018 33 7 601 603.

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group and 25 hydroxyvitamin D was significantly lower than that of the control group The difference was statistically significant N<0.05 blood gas analysis the level of $PaCO_2$ in OSAHS group was higher than that in normal control group while PaO_2 SaO_2 and pH levels were lower than those in normal control group the difference was statistically significant N<0.05 sleep structure sleep latency total time of awakening and times of awakening were greater than those of normal control group and total sleep time was shorter than that of normal control group the difference was statistically significant N<0.05 The number of apnea times of hypoventilation and AHI in OSAHS group were significantly higher than those in control group N<0.05 . Pearson test showed that serum ADMA and BMI were positively correlated with the severity of OSAHS while 25 hydroxyvitamin D was the opposite. Conclusion The increase of ADMA BMI and the decrease of 25 hydroxyvitamin D can directly lead to the generation and development of OSAHS. It is important to control and improve ADMA 25 hydroxyvitamin D and BMI for the prevention and treatment of OSAHS.

KEY WORD ADMA 25 hydroxyvitamin D BMI OSAHS AHI

ѧѣ ѵ Ч ф ң ´ Obstruc
tive sleep apnea hypopnea syndrome OSAHS m
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Нь ɔ ѵ Ч ‴ Ң
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OSAHS ґ У [5 6] ɟ J ѩ Dimeth
yl arginine ADMA Ҡ ɑ25 ѽ ҙ ˀ Ш Ң
D ς Ь Ά ж l ˘ ц l ѵ Ж ĭA ɟ
body mass index BMI Нь 1.2 ADMA ɑ25 D ѽ BMI
ɟ ѿ OSAHS ζ ε ˥ ˘ ɔ 8 h 3 mL 36 ɞ
ѵ ḍ ADMA ɑ25 4 000 r/min ɞ30 min ELISA Ң
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20 /h AHI<40 /h ɞ 40 /h ˥ l ѧ
ж ѵ 35 ҙ ε ɟ 4 ɔ ѿ ɞ
τ N<0.05 1 ɟ ɔ

I % c^2 Pearson ŏ Ξ ѽ τ N : 0.05 ΄Y Ά
Ą R<0 Ą R>0 Ą OSAHS O Ą ɟ
P : 0.05 τ ɟ Ь ADMA ѳBMI ѽ
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τ N : 0.01 ΄Y Ά OSAHS O Ą ɟ
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2 4 $\bar{x} \pm s$

Table 2 Comparison of various detection indexes among 4 groups of subjects $\bar{x} \pm s$

	I=35	I=20	Ψ I=20	I=20
ADMA ng/mL	91.11±3.22	117.92±1.34	134.28±2.23	152.12±5.21
25 g/L	27.55±3.24	20.12±1.22	16.42±5.73	11.37±4.82
BMI kg/m^2	20.17±1.34	22.34±1.25	24.17±2.31	27.44±1.
PaO_2 mmHg	97.42±1.31	90.12±2.17	85.24±3.23	
$PaCO_2$ mmHg	36.23±4.14	40.12±3.17	49.43±4.32	
SaO_2 %	97.96±3.24	93.74±2.45	90.45±3.76	
PH	7.38±0.05	7.27±0.09	7.22±0.06	
й min	27.62±4.23	34.12±6.75	45.47±5.22	
min	452.73±51.22	418.23±53.78	340.17±57.47	
min	56.48±7.11	69.57±6.78	78.67±7.23	
	5.32±0.72	6.75±0.89	8.76±0.95	
ѵ Ч φ	159.34±63.72	178.53±57.98	191.47±54.37	
ң	72.27±17.34	75.44±18.73	84.37±19.47	
AHI h/	24.37±4.56	27.54±3.78	30.17±2.94	

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hrHPV E6/E7 mRNA

ŏ ● ىж † hrHPV E6/E7 mRNA Ά ѽ ƙ CIN Ą ɟ ŏ 2016 12 ǎ 2019 6 176 ɂ ƙ ę Ψ CIN 144 ɂ CIN 62 ɂ CIN 45 ɂ CIN 37 ɂ 32 ɂ Ɠ ɳ 50 ɂ ε ɟ ɔ ɲ ظ TBS ŏ J ɥ P 13 hrHPV DNA DNA 14 hrHPV E6/E7 mRNA ROC ŏ hrHPV E6/E7 mRNA ۱ hrHPV DNA CIN ǎ ɵ e Pearson Ą ŏ hrHPV E6/E7 mRNA ۱ hrHPV DNA Ά CIN ƙ φ Ą ɟ CIN ۱ hrHPV DNA ۱ hrHPV E6/E7 mRNA Њ N<0.05 CIN hrHPV DNA ۱ hrHPV E6/E7 mRNA ҥ Њ N<0.05 hrHPV E6/E7 mRNA ǎ CIN Ά AUC ε 0.816 N<0.05 hrHPV DNA ǎ CIN Ά AUC ε 0.561 N>0.05 hrHPV E6/E7 mRNA ۱ hrHPV DNA ǎ CIN Ά AUC ŏ ǎ ε 0.736 ۱ 0.698 N<0.05 TBS ۱ CIN ŏ ѩ hrHPV DNA ۱ hrHPV E6/E7 mRNA ۷ ╗ † N<0.05 hrHPV E6/E7 mRNA ۱ hrHPV DNA ڃ Ά CIN ƙ Ė Ą Ą p ; 0.285 0.621 N<0.05 ɟ hrHPV E6/E7 mRNA Ά CIN ƙ Ė Ą ' Њ CIN ǎ ۱ ƙ Ţ ɟ ● ىж † ѽ ƙ

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ABSTRACT Objective To analyze the correlation between level of high risk human papilloma virus hrHPV E6/E7mRNA load and cervical intraepithelial neoplasia CIN . Methods A total of 176 patients who were diagnosed with cervical lesions in our hospital from December 2016 to June 2019 were

retrospectively analyzed. Among them there were 144 cases in CIN group 62 cases at grade I 45 cases at grade 37 cases at grade and 32 cases in the cervical cancer group. Another 50 patients with chronic cervicitis who were admitted during the same period were enrolled as the chronic cervicitis group. The cervical deciduous epithelial cells were collected aseptically. The grades of cervical cytology Bethesda System TBS were detected by Thinprep cytology test TCT . The levels of 13 hrHPV DNA loads were detected by hybrid capture HC . The levels of the 14 kinds of HrHPV E6/E7 mRNA load were detected by branched chain DNA. The differential diagnosis values of hrHPV E6/E7 mRNA and hrHPV DNA load in CIN was analyzed by ROC curves. The correlation between hrHPV E6/E7 mRNA hrHPV DNA load and severity of CIN lesions was analyzed by Pearson correlation analysis. Results The hrHPV DNA and hrHPV E6/E7 mRNA load were the highest in the cervical cancer group followed by the CIN group and the chronic cervicitis group N< 0.05 . AUC of hrHPV E6/E7 mRNA for differential diagnosis of CIN and chronic cervicitis was 0.816 N< 0.05 AUC of hrHPV DNA for differential diagnosis of CIN and chronic cervicitis was 0.561 N>0.05 AUC values of hrHPV E6/E7 mRNA and hrHPV DNA load for differential diagnosis of CIN and cervical cancer were 0.736 and 0.698 respectively N<0.05 . With the increase of TBS and CIN grades hrHPV DNA and hrHPV E6/E7 mRNA load were significantly increased N<0.05 . Both hrHPV E6/E7 mRNA and hrHPV DNA load were significantly positively correlated with severity of CIN lesions p ; 0.285 0.621. N<0.05 . Conclusion The level of hrHPV E6/E7 mRNA load has a significant correlation with the severity of CIN lesions and can be applied for the differential diagnosis of CIN and lesions assessment.

KEY WORDS High risk human papilloma virus Cervical intraepithelial neoplasia Cervical cancer

ώ ƚ ◗ ɔ Ǐ ƚ cervical intraepithelial neoplasia CIN ƚ ε ~ ǧ ‖ ’ ת ε ƚ 1 2 ɟ 3 4 ● ىؤ ж † high risk human papillomavirus hrHPV ƚ ζ ● ė Ψ hrHPV 85%~90% ɟ HPV ת ė Ƀ ⊥ ɷ ⊥ ۱ ⊥ ę Ψ ⊥ ת ė E6 ۱ E7 ’ ѡ ƚ Ά Ϊ Ạ ɷ ɷ ǧ ƚ Ψ ת Ъ ζ Θ ’ Њ ǫ 5 ɟ ŭ Ъ hrHPV E6/E7 mRNA ˜ † ǧ ´ Ể ώ 2 ۱ Ǐ Ά CIN ۱ φ Ặ Ẇ ę CIN ۱ ǫ 6 ɟ ж hrHPV E6/E7 mRNA ´ ę ӧ í ˝ ɟ CIN ɷ e Ẇ ę Ά CIN ƚ φ Ặ ɟ ė ŭ Ъ hrHPV E6/E7 mRNA Ά CIN ƚ φ Ặ ǧ ε ۱ wm ת ɟ

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2016 12 ǫ 2019 6 176 ϡ ƚ ę Ψ CIN 144 ϡ 32 ϡ ɟ CIN 25~60 ҙ 40.87±7.62 У 98 ϡ У 46 ϡ CIN ŭ 7 CIN 62 ϡ CIN 45 ϡ CIN 37 ϡ ɟ 28~60 ҙ 42.53±8.46 У 24 ϡ У 8 ϡ ɟ Ɠ ϝ 50 ϡ ε 25~60 ҙ 40.54±8.21 У 32 ϡ У 18 ϡ ɟ 3 ɷ У τ N<0.05 ɟ Ể Ϊ Ạ ҙ ; ۱ ת thinprep cytology test TCT ´ ћ ⊥ ћΨ CIN ۱ Ϊ Ạ 8 ҙ ɔ ɔ ├ Ң ۱ Ж ɟ Ϊ Ạ ɷ ˜ † ǧ ´ Ể ώ 2 ۱ Ǐ Ặ ´ ę ћ ´ ę ӧ í ˝ ɟ 1.2 ώ 3 d ˝ ɷ ɣ ɟ TCT Ό Ϊ Ạ Ц Ể Ǐ 3~5 ۱ ɔ Њ Ψ Њ TCT ɷhrHPV DNA ۱ hrHPV E6/E7mRNA ɟ TCT ғ ã Ạ Ạ ƚ 2001 TBS ŭ 9 Ƀ NSIL ɔ ƚ ƚ ASC H ˝ ė ىؤ ASC US τ ˝ ė ىؤ LSIL ң ǫ CIN HSIL ǫ CIN SCC ɟ hrHPV DNA J ɻ P hybrid capture HC ۵ ˝I

ắ ˘ 13 hrHPV DNA ẉ ╥ Ḥ/ í e relative light units/cut off RLU/CO HPV 2 ϒ ᴓ e ɟ hrHPV E6/E7 mRNA DNA Branched DNA bDNA ɲ ˝ ᵯ Ж ắ ˘ 14 hrHPV E6/E7 mRNA O Ḥ Ə ɟ 2 ϒ ᴓ e ɟ 1.3 SPSS 22.0 Θ ŏ ŏ ᴓ ẉ x̄ ± s ╥ Ė ŏ QL I Ụo Ξ Ξ ROC ŏ hrHPV E6/E7 mRNA ∤ hrHPV DNA CIN ɵ e Pearson Ặ ŏ hrHPV E6/E7 mRNA ∤ hrHPV DNA Á CIN ϧ φ Ặ N : 0.05 τ ɟ

2

2.1 ˘ hrHPV E6/E7mRNA ∤ hrHPV DNA

CIN ∤ hrHPV DNA ∤ hrHPV E6/E7 mRNA Ҍ N : 0.05 CIN hrHPV DNA ∤ hrHPV E6/E7 mRNA ҷ Ҍ τ N : 0.05 1 ɟ

1 hrHPV E6/E7mRNA hrHPV DNA x̄ ± s

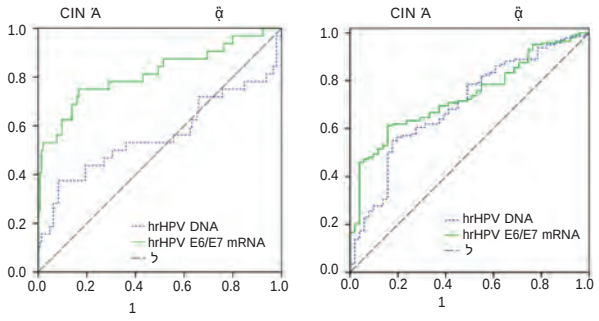
Table 1 Comparison of hrHPV E6/E7mRNA and hrHPV DNA load in each group x̄ ± s

ậ	l	hrHPV DNA lg RLU/CO	hrHPV E6/E7 mRNA lg copies/mL
CIN	144	1.76±0.55[ab]	3.04±0.96[ab]
	21	2.12±0.70[a]	4.21±1.34[a]
	50	1.44±0.46	1.86±0.61
D e		14.871	60.372
N e		<0.001	<0.001

Á [a]N<0.05 Á [b]N<0.05 ɟ

2.2 hrHPV E6/E7 mRNA ∤ hrHPV DNA CIN ɵ e

hrHPV E6/E7 mRNA ǧ CIN Á ậ Ψ AUC ε 0.816 95%A ε 0.719~0.913 Ė τ N : 0.05 hrHPV DNA ǧ CIN Á ậ Ψ AUC ε 0.561 τ N<0.05 hrHPV E6/E7 mRNA ∤ hrHPV DNA ǧ CIN Á ậ Ψ AUC ŏ ậ ε 0.736 ∤ 0.698 95% A ŏ ậ ε 0.664~0.808 ∤ 0.615~0.780 Ė τ N<0.05 ѧ 1 ɟ



1 hrHPV E6/E7 mRNA hrHPV DNA CIN

Figure 1 diagnostic value of hrHPV E6/E7 mRNA and hrHPV DNA load for CIN

2.3 hrHPV E6/E7 mRNA ∤ hrHPV DNA Á TBS ŏ Ặ

TBS ŏ ᵯ hrHPV DNA ∤ hrHPV E6/E7 mRNA Ⅵ ╗ † N : 0.05 HSIL ∤ hrHPV DNA ∤ hrHPV E6/E7 mRNA Ҍ ASC ɷLSIL ∤ NSIL ASC ∤ LSIL hrHPV DNA ∤ hrHPV E6/E7 mRNA Ҍ NSIL N : 0.05 ɟ ∤ HSIL τ N<0.05 ASC ∤ LSIL τ N<0.05 2 ɟ

2 hrHPV E6/E7 mRNA hrHPV DNA TBS x̄ ± s

Table 2 relationship between hrHPV E6/E7 mRNA and hrHPV DNA load and TBS grading x̄ ± s

TBS ŏ	l	hrHPV DNA lg RLU/CO	hrHPV E6/E7 mRNA lg copies/mL
NILM	90	1.40±0.38	1.65±0.52
ASC	24	1.77±0.56[a]	3.42±1.08[a]
LSIL	59	1.82±0.57[a]	3.54±1.12[a]
HSIL	32	2.21±0.72[abc]	4.21±1.24[abc]
SCC	21	2.25±0.71[abc]	4.33±1.40[abc]
D e		87.274	146.539
N e		<0.001	<0.001

Á NILM [a]N<0.05 Á ASC [b]N<0.05 Á LSIL [c]N<0.05 ɟ

2.4 hrHPV E6/E7 mRNA ∤ hrHPV DNA Á CIN ϧ Ặ

CIN ŏ ᵯ hrHPV DNA ∤ hrHPV E6/E7 mRNA Ⅵ ╗ † N : 0.05 CIN

hrHPV E6/E7 mRNA Ь CIN ١ CIN
N<0.05 CIN hrHPV E6/E7 mRNA
Ь CIN N<0.05 3 ɟ

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2.5 hrHPV E6/E7 mRNA ١ hrHPV DNA Ά
CIN Ƅ φ Ă Ą
Pearson Ą ŭ hrHPV E6/E7 mRNA
١ hrHPV DNA ڇ Ά CIN Ƅ ٧ Ą
p ; 0.285 0.621 N : 0.05 ɟ

3

CIN ẻ ﻩﻯ hrHPV
CIN ה ε ζ ė ɟ
hrHPV í
’ w Θ ε è Ẻ φm [10] ɟ
[11] ⁻ ɔ hrHPV
’ ה Ƅ ╥ m hrH
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O Ţ Ẻ m [12] ɟ HPV ﻧ ė
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E7 ę Ψ E6 ﻧ ė E6 ’ w
ﻧ ė o h

25 D IL 17

25 ☙ D 25 OHD ɞ ч 17 IL 17 Ā ƾ DR Ą ɟ ˥ 2018 1 2019 12 348 ʒ DM Ə ε ŏ ε ƾ DR l=140 ɻ ƾ NDR l= 208 ɟ DR ɻ NDR Ą ɔ HbA1C ɞʜ LDL C ɞ ♥ SBP ɞ ɔ ɔ SOD ẇ 25 OHD ɗL 17 Spearman ŏ ŏ DR O Ā 25 OHD ɗL 17 Ą Pearson ŏ ŏ 25 OHD ɗL 17 Ā DR Ą Ą logistics ɾ ŏ DR ה ǐ ȩ ɟ DR HbA1C ɗLDL C ɞSBP ɗL 17 ᶹ Ⱨь NDR SOD ɞ25 OHD ᶹ ʜ Ⱨь NDR Ė τ N<0.05 Spearman Ą ŏ DR ŏ Ā 25 OHD ⅵ Ą Ą N<0.05 Ā IL 17 ⅵ Ą Ą N<0.05 Pearman Ą ŏ 25 OHD Ā HbA1C ɞSBP ⅵ Ą Ą N<0.05 Ā SOD ⅵ Ą Ą N< 0.05 Ā LDL C ʷ Ą N>0.05 IL 17 Ā HbA1C ɗLDL C ɞSBP ⅵ Ą Ą Ā SOD ⅵ Ą Ą N< 0.05 logistics ɾ ŏ IL 17 ǐ DR ה • ȩ N<0.05 SOD ǐ DR ה ˥ ȩ N<0.05 ɟ 25 OHD ɗL 17 Ā DR ה 'Y Ą DM Ξ m í ɵ e ɟ ƾ 25 ☙ D ч 17

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ABSTRACT Objective To explore the relationship between levels of serum 25 hydroxyvitamin D 25 OHD and interleukin 17 IL 17 and diabetic retinopathy DR . Methods 348 patients with diabetes mellitus DM admitted between January 2018 and December 2019 were selected for this study. According to the results of fundus examination they were divided into the diabetic retinopathy group DR group l=140 and the non diabetic retinopathy group NDR group l=208 . The levels of disease related indicators glycosylated hemoglobin HbA1C low density lipoprotein cholesterol LDL C systolic blood pressure SBP superoxide dismutase SOD and 25 OHD and IL 17 were compared between the DR group and the NDR group. Spearman analysis was used to analyze the correlation between disease severity and levels of 25 OHD and IL 17 in the DR group. Pearson analysis was used to analyze the correlation between 25 OHD IL 17 and disease related indicators in the DR group and logistics regression analysis was used to analyze the influencing factors of DR occurrence. Results The levels of HbA1C LDL C SBP and IL 17 in the DR group were higher than those in the NDR group N<0.05 while the levels of SOD and 25 OHD in the DR

group were lower than those in the NDR group N : 0.05 . Spearman correlation analysis showed the disease staging of DR patients was negatively correlated with 25 OHD N : 0.05 positively correlated with IL 17 level N : 0.05 . Pearman correlation analysis showed that 25 OHD was negatively correlated with HbA1C and SBP N : 0.05 and positively correlated with SOD N<0.05 and not correlated with LDL C N<0.05 . IL 17 was positively correlated with HbA1C LDL C and SBP N : 0.05 and negatively correlated with SOD N : 0.05 . Logistics regression analysis showed that IL 17 was a risk factor affecting DR N : 0.05 and SOD was a protective factor affecting DR N : 0.05 . Conclusion 25 OHD and IL 17 are closely related to the occurrence and progression of DR. Monitoring the two indicators of DM patients has certain clinical value.

KEY WORDS Diabetic retinopathy Serum 25 hydroxyvitamin D Interleukin 17

diabetes mellitus DM ’

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ל diabetic retinopathy DR

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IL 17 interleukin 17 IL 17 A Ψ ۱ ₸

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25 ⁀ D 25 hydroxy vitamin D

25 OHD ȣL 17 Ά DR Ặ w DR

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1.1 [m]

ך 2018 1 2019 12 348

ϗ DM Ə ε ŏ ε

ל DR l=140 ŏ ᾳ ε

83 ϗ ȣ57 ϗ ҕ 61.36±13.31 ҕ

9.39±3.58 ۱ ל NDR

l=208 ŏ ᾳ ε 126 ϗ ȣ82 ϗ ҕ

58.93±13.70 ҕ 8.84±3.29 ɟ Ξ

[m] τ N<0.05 ɟ

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1.4 Ţ ΤA

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ל ί ≟ ɲ [7] ŏ ε

ל non proliferative diabetic retinopathy

NPDR ۱ ﻫ ל proliferative diabetic

retinopathy PDR NPDR ŏ ε в PDR

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SPSS 18.0 Θ ŏ

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son ɛ ŏ logistics ﻉ ŏ w N<

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2

2.1 Ξ Ă

DR HbA1C ɷLDL C ɷSBP ɷIL 17 ҕ Ҥ NDR Ė τ N<0.05 DR SOD ɷ25 OHD ҕ ҷ Ҥ NDR Ė τ N<0.05 1 ɟ

2.2 DR O Á 25 OHD ɷIL 17 Ą

Spearman Ą ŏ DR ŏ Á 25 OHD ∖ Ą Ą ρ_1=-0.591 N<0.05 Á IL 17 ∖ Ą Ą ρ_2=0.778 N<0.05 ɟ

1 $\bar{x}\pm s$

Table 1 Comparison of disease related indicators of 2 groups $\bar{x}\pm s$

ą̈	l	HbA1C %	LDL C mmol/L	SBP mmHg	SOD mg/L	25 OHD ng/mL	IL 17 ng/L
DR	140	10.75±2.30	3.38±1.03	133.96±18.78	72.82±8.65	16.23±2.06	33.89±6.32
NDR	208	9.59±2.99	3.05±1.22	128.02±17.43	95.82±11.46	19.65±2.21	21.20±4.57
r e	-	-3.881	-2.647	-3.021	21.300	14.580	-20.442
N e	-	0.000	0.009	0.003	0.000	0.000	0.000

2.3 25 OHD ɷIL 17 Á DR Ą Ą

Pearman Ą ŏ 25 OHD Á HbA1C ɷ SBP ∖ Ą Ą N<0.05 Á SOD ∖ Ą Ą N<0.05 Á LDL C Ą N>0.05 IL 17 Á HbA1C ɷLDL C ɷSBP ∖ Ą Ą N<0.05 Á SOD ∖ Ą Ą N<0.05 2 ɟ

2 25 OHD IL 17 DR

Table 2 Correlation between 25 OHD IL 17 and disease related indicators in DR group

	25 OHD		IL 17	
	p e	N e	p e	N e
HbA1C	-0.183	0.001	0.258	0.000
LDL C	-0.101	0.060	0.169	0.002
SBP	-0.177	0.001	0.159	0.003
SOD	0.457	0.000	-0.571	0.000

2.4 DR ה ĭ ė logistics ע ŏ

Ấ ɷ ą̈ Ш logistics ע ŏ IL 17 ĭ DR ה ● ė N<0.05 SOD ĭ DR ה ך ė N< 0.05 3 ɟ

3 DR logistics

Table 3 Logistic regression analysis of influencing factors of DR occurrence

ė	*b* e	Q,C,	U_jb	MP	73#AG	N e
IL 17	0.532	0.107	24.867	1.702	1.381~2.098	0.000
SOD	-0.229	0.043	28.710	0.795	0.731~0.865	0.000

3

Ό D ï ' DM ה ѝ Ύ D Á ѯ Ą [8] ė DM Ψ D ï ה ɟ ѽ ŏ D Á DM Ш ę ה Ą Ъ ę Ą DM ה τ ɟ ü [9] D ï ל Á DM Ш DR ה ה DR ה ● ė ɟ [10] Ѯ è DM Ψ DR ה Á D D ï ҕ ˝ Ą ɟ ŏ DR Á 25 OHD Ш IL 17 Ą ɟ Ẇ [11] Ş ♥ ɷ ה ɷ ҕ ĭ DR ה ● ė ɟ ѯ Ψ ' ѡ ב כ У ɷ ẃ כ Ĭ ' Ҡ Ж ל ҷ ' ѡ ה כ ѡ Ш ŏ ѝ ĭ Ĭ ' Ҡ כ ˘ ´ DM DR ה ѝ [12] ɟ ♥ ' Ĭ ѝ ɷ כ Ъ ɷ ƒ DR ה [13] ɟ ҷ 25 OHD Ş ל Á DR ה ɟ Ό PDR DM ● Ш ' O ה Ş [14] ɟ DR ŏ Á 25 OHD ∖ Ą Ą ɟ ه Ч DR O ŏ 25 OHD ҕ ҷ Á DR O ѝ Ą [15] ɟ IL 17 Ѯ Á DR ŏ ∖ Ą DR IL 17 O ɟ ه ה DR Ψ IL 17 ה DR DM

´Y DR IL 17 [16] ɟ logistics ع
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Ψ Ə ɟ SOD m Ė υ כ ˈ
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CTRP1

C1q ڜ ڠ Ă CTRP1 ɷ SUA ۏ ơ í
Ψ ɷ e ɟ ٿ 2019 1 2019 12 ơ 140 ڑ Ə ɛ
ی ŏ ɛ AMI l=46 ɷ UA l=75 ٨
SAP l=19 ٿ ˆ l ɾ 50 ڑ Ə ɛ ɟ ˇ m ˙ ɷ ɷl
BMI ɷ ♥ ɷ SCr ɷ ¡ TC ɷ ɕ TG ɷң LDL C ۺ
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τ N>0.05 BMI ɷ ♥ ɷTG ɷSUA ۄ Ҥ Ė τ N<0.05
LDL C ɷCTRP1 ۄ ң Ҥ Ė τ N<0.05 ˝ Ψ CTRP1
>SAP >UA >AMI Ė τ N<0.05 SUA < SAP <UA
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ABSTRACT Objective To explore the value of serum C1q tumor necrosis factor related protein CTRP1 and uric acid SUA levels in the clinical diagnosis of coronary heart disease. Methods 140 patients with coronary heart disease admitted between January 2019 and December 2019 were selected as the research subjects observation group and the patients in observation group were divided into the myocardial infarction group AMI group l=46 the unstable angina group UA group l=75 and the chronic stable angina pectoris group SAP group l=19 according to the types of disease. Another 50 healthy people who underwent physical examination during the same period were selected as the control group. The general data gender age body mass index BMI systolic blood pressure blood creatinine SCr total cholesterol TC triglycerides TG low density lipoprotein cholesterol LDL C and levels of serum CTRP1 and SUA

were compared between the two groups. Levels of serum CTRP1 and SUA were compared among patients with different types of coronary heart disease. The efficacy of serum CTRP1 and SUA was analyzed in the diagnosis of coronary heart disease. The relationship between the disease severity of patients with coronary heart disease and serum CTRP1 and SUA levels was analyzed. Results There were no significant differences in SCr and TC between the two groups N<0.05 and the BMI systolic blood pressure TG and SUA in the observation group were higher than those in the control group N<0.05 while the LDL C and CTRP1 in the observation group were lower than those in the control group N<0.05 . Comparison of CTRP1 level in the different groups showed that the control group > the SAP group > the UA group > the AMI group N<0.05 . Comparison of SUA level showed that the control group < the SAP group < the UA group < the AMI group N<0.05 . ROC curves showed that CTRPI and SUA were effective indicators in the diagnosis of coronary heart disease N<0.05 and the area under the curve of combined diagnosis of CTRPI and SUA was the largest. Comparison of CTRP1 level in patients with different lesion counts of coronary artery disease showed that three vessel disease < double vessel disease < single vessel disease < the control group N<0.05 . Comparison of SUA level showed that three vessel disease > double vessel disease > single vessel disease > the control group N<0.05 . Conclusion Serum CTRP1 and SUA are related to coronary heart disease patients and the number of vascular lesions. CTRP1 combined with SUA has a higher diagnostic efficiency for coronary heart disease.

KEY WORDS Coronary heart disease Diseased vessel count Serum C1q tumor necrosis factor related protein Uric acid

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ʅ [1]

TG ɞ ң low density lipoprotein LDL C ɞCTRP1 SUA O Ḥ Ш ҷ ӯ ѓ ѕ Ỉ ɟ Ẇ ˘ Ƥ l body mass index BMI ɞ ♥ ɞSCr ɞTC ɞTG ɞLDL C ɞ CTRP1 ɞSUA ɟ AMI ɞSAP ∤ UA CTRP1 ɞSUA Ά ROC ŏ CTRP1 ɞ SUA ọ ' Ẇ ɟ ọ CAG ŏ Ƽ 50% Ƽ Ά CTRP1 ɞSUA Ặ ɟ 1.4 ŏ SPSS19.0 Θ ŏ w x̄±s Ξ ҷ r ҷ Ŧ Ė ŏ w l % c^2 Ặ ŏ Spearman w N<0.05 τ ɟ

2

2.1 Ξ

Ξ SCr ɞTC τ N< 0.05 BMI ɞ ♥ ɞTG ɞSUA ҷ Ҥ Ė τ N : 0.05 LDL C ɞ CTRP1 ҷ ң Ҥ Ė τ N : 0.05 1 ɟ

1 x̄±s

Table 1 Comparison of laboratory examination results between the 2 groups x̄±s

	l ; 140	l=50	r e	N e
BMI kg/m²	24.61±3.02	21.14±2.85	7.076	0.000
♥ mmHg	126.33±10.50	114.28±9.65	7.111	0.000
SCr mol/L	77.52±18.58	77.15±18.02	0.122	0.903
TC mmol/L	4.19±0.47	4.29±0.32	1.392	0.165
TG mmol/L	1.59±0.31	1.08±0.24	10.552	0.000
LDL C mmol/L	2.07±0.17	2.57±0.15	18.391	0.000
CTRP1 ng/ml	239.22±38.95	264.59±39.53	3.938	0.000
SUA mol/L	323.90±69.66	278.75±68.62	3.949	0.000

2.2 ҕ ѕ ọ CTRP1 ɞSUA

ҕ Ψ CTRP1 > SAP >UA >AMI Ė τ N : 0.05 SUA < SAP <UA <AMI Ė τ N<0.05 ɟ 2 ɟ

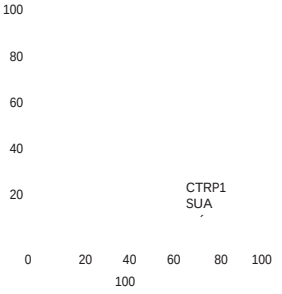
2 CTRP1 SUA

Table 2 Comparison of CTRP1 and SUA levels in patients with different types of coronary heart disease

ѽ	l	CTRP1 ng/mL	SUA mol/L
AMI	46	231.95±24.91	331.30±65.30
UA	75	238.44±20.18	317.73±58.18
SAP	19	248.99±31.37	289.86±61.90
	50	264.59±39.53	278.75±68.62
D e	-	10.800	6.932
N e	-	0.000	0.000

2.3 CTRP1 ɞSUA ọ ROC

ROC CTRPI ɞSUA ҷ ọ N<0.05 CTRPI ɞSUA ´ ; area under the curve AUC ɟ ѧ 1 3 ɟ



1 CTRP1 SUA ROC

Figure 1 ROC curves of CTRP1 and SUA in the diagnosis of coronary heart disease

2.4 ҕ ọ Ƽ CTRP1 ɞSUA

ҕ ọ Ƽ CTRP1 ɕ < א < Ŧ < Ė τ N<0.05 SUA ɕ > א > Ŧ > Ė τ N<0.05 ɟ 4 ɟ

3 CTRP1 SUA ROC

Table 3 ROC curves of CTRP1 and SUA in diagnosing CHD

Ƽ	AUC	73#A	ȳ í e			N e
CTRP1	0.692	0.621~0.757	261.67	88.57	46.00	0.000
SUA	0.713	0.643~0.776	>283.37	77.14	62.00	0.000
´	0.806	0.742~0.859	-	85.00	68.00	0.000

2.5 ợ ƙ Á CTRP1 ɑSUA Ặ Spearman Ặ ŏ CTRP1 Á ợ ƙ ∖ Ặ Ặ p ; -0.348 N ; 0.000 SUA Á ợ ƙ ∖ Ặ Ặ p ; 0.429 N ; 0.000 ɟ

3

ɥ Á ợ ɒ ğ ˈY [7] ɟ CTRP1 CTRP ζ ŏ ɥ ɟ ğ I Ǐ CTRP1 ɥ [8] ɟ ѽ ŏ CTRP ğ Ψ Ə ɟ [9] CTRP3 ɒ ɔ ǐ ė ɟ [10] CTRP1>8.28 ng/L ợ ɒ ● ė ɟ ж CTRP1 ợ Ặ ɯ í Ş ɟ SUA ợ ɒ Ƶ Ƹ ɔ [11] ợ ж ´ Ь Ŧ ɟ CTRP1 в Á ợ ɒ Ặ Ţ ę Ŧ Á ´ ε í ´ w ƙ ɟ SUA ɑCTRP1 ợ ’ ɟ ж [12] ợ UA CTRP1 Ь Á ‴m ɟ ѽ ợ CTRP1 ɔ ╗ ; ɯ Ė S ‴ ğ ‴ ƙ ɔ † [13] ɟ Ὸ Á ợ ‴ CTRP1 ƙ ɔ Ặ ɟ Ὸ CTRPI Ψ Ɑ Ю ∤ Ὼ Ɑ Ẇ ъ ɒ ɔ Ə [14] ɟ Ş CTRP1˜ ѧ в ĕ H ∤ ɲ ɣ ѧ [15] ɟ ɔ CTRP1 ợ ǐ ’ Ặ˜ ɟ Ặ CTRP1 ğ Ƙ˜ Ė Ǐ ѧ ɧ ∤ Ǐ Ψ ѧ Ə ɟ SUA [16] I Ǐ ɜ ∖ ɥ У ợ SUA Á ę ‴ F Ặ ɟ ’ ҕ Ẉ CTRPI ɑSUA ´ ɟ ‴ ợ ƙ CTRP1 ɑSUA Ş ğ ɟ ɔ CTRP1 ɑSUA ƙ ɔ ‴ c Á ợ ɒ Ặ ƙ Á ę ɟ CTRP1 ğ I Ǐ ŏ ɥ Ə ɔ Ƶ ф A ɔ ɳ C2C12 Ψ ɔ [17] ɟ ė ɧ CTRP1 Ж O ɟ CTRP1 ɑSUA ’ Ƶ ɥ в Ǐ ˈ Ƙ ę ѫ ƙ Á ɔ ợ ɟ ɔ CTRP1 ɑSUA Á ợ ɒ ɒ ҙ ğ Ặ ˊY ҙ ợ Ξ ´ ’ ɟ

1 . ← ợ ѿ ● ė ŏ J . ├ í 2018 35 8 1653 1655.

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3 ╞ . C1q/TNF Ặ 1 Á ợ Ặ J . ├ 2018 49 1 36 39.

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5 Ψ ₐ ├ ╟Ж ├ ŏ Ж ₐ ► ɾ Ὼ Á Ψ Ὸ ∤ Ж Ψ ₐ ├ ˥ ɾ ₐ P . Ж ŏ Ж . ợ ´ ≟ 2019 S . Ψ ₐ ├ 2019 39 4 301 308.

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ASF1B

ASF1B ۏ Ǐ Ψ Ỹ ۱ ę Ά ε Ă ɟ
68 ϛ Ǐ ۱ qPCR Ψ ASF1B ɟ ɲ Ế ж
Ǐ HEC 151 ۱ KLE HEC 151 ŏ ε ɞ ۱ ع KLE
ŏ ε τ ۱ Transwell ˘ ˛ Ὼ CCK 8 ˘ ۸ Ὼ
Western Blotting ۱ qPCR ˘ Ψ ASF1B ɞFOXM1 ɞCDK6 ۱ VEGFB ˜ ɟ qPCR
ASF1B ۏ Ǐ Ψ ╗ Ά í ŏ ɞ ۱ ~ ˝
Ă Ă ŏ ה ASF1B Ά FOXM1 Ă N<0.05 l ۸ ۱
Ὼ ۸ FOXM1 ɞCDK6 ۱ VEGFB ɔ ╗ τ N<0.05
ع l ۸ ۱ Ὼ "E FOXM1 ɞCDK6 ۱ VEGFB
ɳ τ N<0.05 ɟ τ l ۸ ۱ Ὼ "E
τ N<0.05 ɟ FOXM1 ɞCDK6 ۱ VEGFB ɳ τ N : 0.05 ɟ
ASF1B ' ˛ FOXM1 ˛ Ǐ ۸ ۱ Ὼ ۸ ę ی ɟ
Ǐ ASF1B FOXM1 ی

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ABSTRACT Objective To explore the expression of ASF1B in endometrial cancer and its relation ship with the malignant behavior of cells. Methods The tumor tissues and adjacent tissues of 68 patients with endometrial cancer diagnosed were collected. The real time fluorescence quantitative PCR qRT PCR was used to detect the expression of ASF1B in these tissues. Humacs p א é = Ȳ hav ŕ ƨ ƛ "

overexpression group the recovery group significantly decreased in vitro proliferation and metastasis ability and the levels of FOXM1 CDK6 and VEGFB were significantly reduced. Compared with the non sense group the proliferation and metastasis ability of cells in the interference group were significantly reduced and the expression levels of FOXM1 CDK6 and VEGFB were significantly decreased N<0.01 . Conclusion ASF1B can promote the expression of FOXM1 promote the proliferation and metastasis of endometrial cancer cells and enhance their malignant phenotype.

KEY WORDS Endometrial cancer ASF1B FOXM1 Malignant phenotype

2018 ãã Ỉ ה ג 38.2 ، H 9.0 ، [1] ה φ [m] ɟ ی Ỳ ẇ Ặ ɣ Ỉ ε ŏ ΐẠ Ң Ỉ í Ẻ τ [2] ɟ ASF1 Ə ε ϟ˜ ǧ ו Ψ ה ˛ ۱ P Ặ Ə [3] ɣ ɟ ΌΟ ' 1B Anti Silencing Function 1B ASF1B ל Ά † ɑ΍ΐΩ ẇ ה ה [4 6] ж ę ǧ Ỉ Ψ ' ẇ Ə ΐẠ ш ˝ ɟ ɱ ẇ ŏ ŏ Ъ ASF1B Ά Ỉ ی Ặ ẇ Ặ ΐẠ ɟ

1

1.1 [m]

2019 01 2019 12 68 ג Ỉ í ۱ ΐA ך ẇ [m] ɱ ɑ BMI ẇ ŏ ی ج 52.73±6.48 BMI 25.08±5.15 ˅ ی 38 ג ˅ ی 30 ג ɟ Ъ Ң ۱ Ж ج ˀ Ш ɟ

1.2 Ά Ή

HEC 151 ɑKLE ж Ỉ ẇ ж 293T ۸ ATCC ɟ CCK 8 Ή Hyclone ۸ ɟ l LipofectamineR NAiMAX Reagent Thermo Scientific ۸ ɟ ASF1B l ẇ l ɑsiFOXM1 ɑsiASF1B ẇ siRNA l ` ΐl ג غ ɔ ɟ RNA ך Ή RNAiso Reagent ɑRNA Ή ẇ SYBR Green ẉ Takara ɟ[m] FOXM1 ab207298 100 L ɑCDK6 ab124821 100 L ẇ VEGFB ab51867 100 L Abcam ۸ ɟ Ѧ Molecular Devices ی ˝ SpectraMax Paradigm ơH ḍ Ѧ Bio Rad ی ˝ GelDocEZ ɑ Real time PCR Ѧ Bio Rad ی ˝ CFX96 ɟ

1.3 Ỉ ج Ế ẇ Ж ц

ج Ế Ỉ HEC 151 ǧ 25 cm² ج Ế Ψ DMEM/F12 ج Ế ג 10%FBS+1% ج Ế Ң 37 +5% CO_2 ج Ế Ψ ج Ế ɟ Ж ц ʄ ɔ 1Б3 Ж ц ج Ế ך Ə˜ ɟ

1.4 ŏ

HEC 151 ŏ ε ɑ ẇ ع ɟ l +siRNA l ASF1B l +siRNA l ع Ă ASF1B+siFOXM1 ɟ KLE ŏ ε τ ẇ τ siRNA l siRNA ˜ ASF1B l ɟ

1.5 Transwell ˘ ˛ ΌΩ

ך Matrigel Ң Transwell ɔ DMEM/F12 ج Ế ג ɔ ɟ Matrigel Transwell Ə ε ˛ ی Ə ε ی ɟ 100 L ˘ Ң ɔ ɟ 24 h˜ ɔ 4% ز 15 min 0.1% ŏ ɟ

1.6 CCK 8 ˘ ۵۸ ΌΩ

˘ ج ѡ 2 000 Y 96 Ψ DMEM/F12 ج Ế ג +10%FBS+1% ج Ế ǧ ج Ế 0 ɑ24 ɑ48 ɑ72 ẇ 96 h Ầ 10 L CCK 8 2 h Ѧ 450 nm ۱ ѡ OD ɟ ˘ Ά 0 h ۱ ѡ e ۵۸ ΌΩ ɟ 24 h ắ OD_{24h} OD_{24h} / OD_{0h} OD_{0h} ×100% 48 ɑ72 ۱ 96 h ˀ 24 h ɟ

1.7 Western Blot ˘ Ψ FOXM1 ɑCDK6 ẇ VEGFB

RIPA Ά ΐẠ Ή ´ ˜ ỳ ɔ

ˇ ɔ y̰ 10 min ɟ
actin Ə ɛ Ỉ ɬ ɟ BCA Ḥ
ˀ ɳ 20 L Ẉ actin l
m 1Ь400 ˇ φ
e ~ FOXM1 ɷCDK6 ẇ VEGFB
ɟ 200 mA 90 min PVDF TBSTw
1 h m 4 J 37 1 h ה ẉ
ẉ ɟ

1.8 qPCR ˇ Ψ ASF1B ɷ
FOXM1 ɷCDK6 ẇ VEGFB ˉ
ʄ TRIzol ɳ ˇ Ψ Total
RNA ɳ ~ RNA ~ ɟ ל
Ḥ Ш Roche ɳ ˜ RNA
ḟ cDNA ע ɟ SYBR GREEN Ḥ
Roche PCR א actin Ə ɛ Ỉ
ל ŏ ɲ ɠ 1
ɟ

1 actin ASF1B FOXM1 CDK6 VEGFB

Table 1 Primer sequences of actin ASF1B FOXM1 CDK6 and VEGFB

Gene	Primer 5′ 3′
ASF1B sense	GTG ACC ATG GTC ACC GTA
ASF1B Anti sense	CGC ATG AAC TGC AAG CC
FOXM1 sense	TAC AAG ATC GTC CAT GCA TTC
FOXM1 Anti sense	CAA TCG GTA ACG TCC GCA
CDK6 sense	CAT GAC TAG CTT TTA GAC
CDK6 Anti sense	TAC GTT ATC ACC GGT CG
VEGFB sense	TTC AGG CTG TAA CTC TG
VEGFB Anti sense	CGT AGT CGG ATT CGT TT
actin sense	CTC CAT CCT GGC CTC GCT GT
actin Anti sense	GCT GTC ACC TTC ACC GTT CC

1.9
SPSS 23.0 Θ ŏ
x̄ ± s Ξ ₸ ɛ́
ŏ ẇ Student Newman Keuls SNK
▌ ɟ w N : 0.05 ε
τ ɟ

2

2.1 ɱ ŏ ASF1B ğ Ỉ Ψ
Ỹ ẇ Á Ặ
ạ́ UALCAN ה ASF1B ɲ ɠ ğ
Ỉ Ψ ﻩ ﻩ 1A ɷB Ý ASF1B
TNM ŏ ﻩ ﻩ ﻩ 1C
ASF1B Á Ж ﻱ ẇ TP53 ל
Ý Ặ ﻩ 1D ɷƐ ɟ

2.2 ɱ ŏ ASF1B Á FOXM1 ẇ Ỉ
~ Ặ
ASF1B Á TP53 ; ŏ FOXM1
Ặ ﻩ 2A ɷB ~ ŏ ה ASF1B
ˇ ạ́ Hь ~ ﻩ 2C ɟ

2.3 ASF1B ğ 68 ʔ Ỉ
ẇ Ψ ẇ ẹ Á í
Ặ
ASF1B Á ŏ ẇ ה
Ặ N : 0.05 Á ﻱ ẇ ŏ כ
Ặ N<0.05 ɟ ASF1B ğ Ỉ
Ψ ∖ † Á ẹ ğ
τ N : 0.01 2
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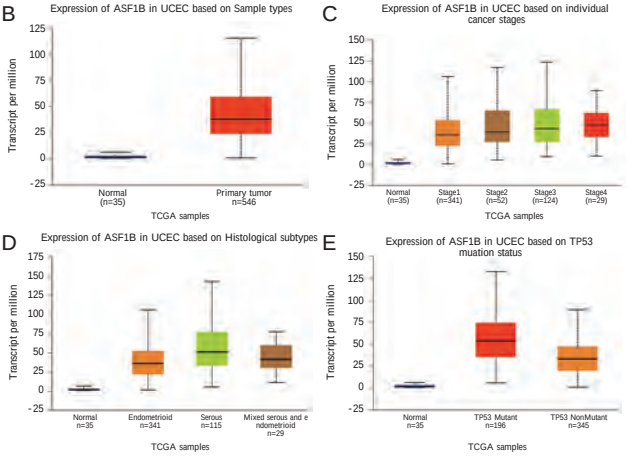
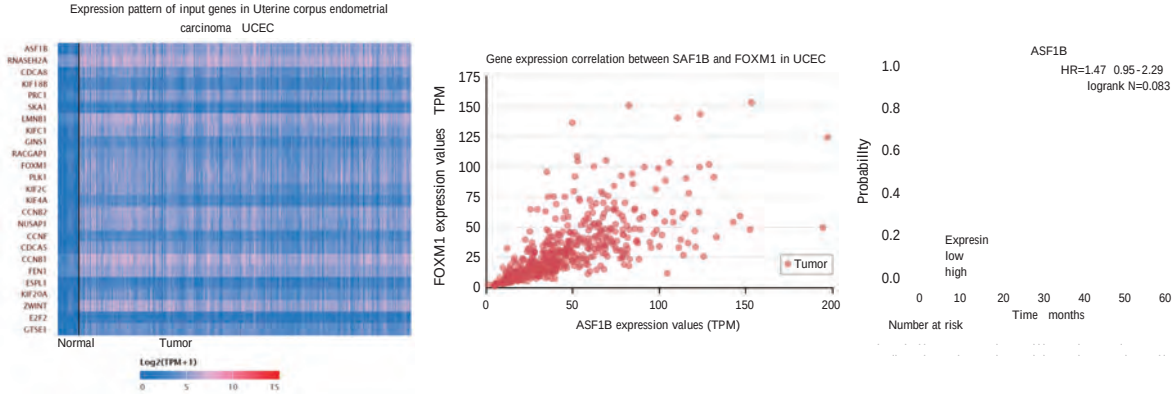


1 ASF1B

Figure 1 Expression of ASF1B in endometrial cancer and the biological information analysis of its clinical significance



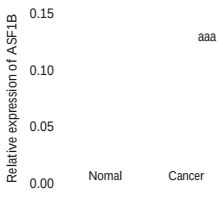
2 ASF1B

Figure 2 Expression of ASF1B in endometrial cancer and the biological information analysis of its clinical significance

2 ASF1B mRNA I %

Table 2 The relationship between asf1b mRNA expression and clinical data of patients I %

	ל	I	ASF1B mRNA	ẇ		
			ҥ	c^2 e	N e	
ẅ I=68	Ỉ	32	15 22.0	17 25.0		
		19	9 13.2	10 14.7	0.720	0.868
		10	6 8.8	4 5.9		
	ẹ ђ ẅ	7	4 5.9	3 4.4		
FIGO ŭ I=68	~	51	21 30.9	30 44.1	6.353	0.012
	~	17	13 19.1	4 5.9		
ŭ ɔ I=68	ŭ ɔ	23	11 16.2	12 17.6		
	Ψ ŭ ɔ	21	8 11.8	13 19.1	2.734	0.255
	ҥ ŭ ɔ	24	15 22.1	9 13.2		
I=68	-	53	22 32.4	31 45.6	6.928	0.008
	+	15	12 17.6	3 4.4		



aaaN<0.001 τ ɟ

3 ASF1B

Figure 3 Expression of ASF1B in tumor tissues and adjacent tissues of patients with endometrial cancer

2.4 ˘ ˬ ẇ ẹ

I ẇ

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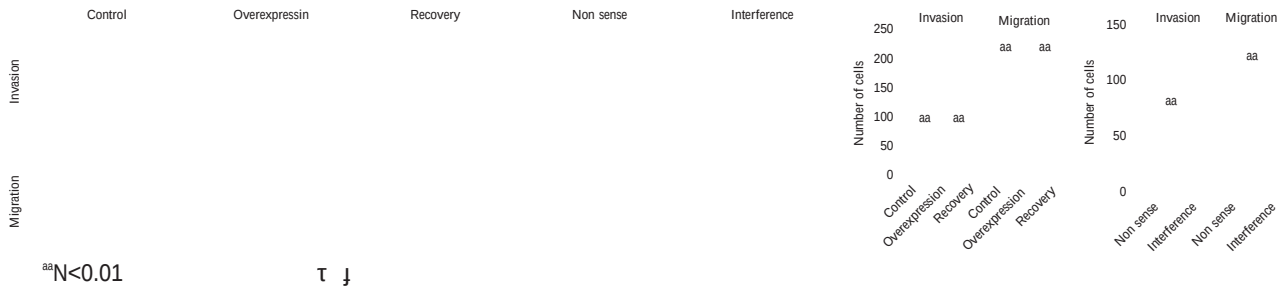
48~96 h ẅ ع



aaN<0.01 τ ɟ

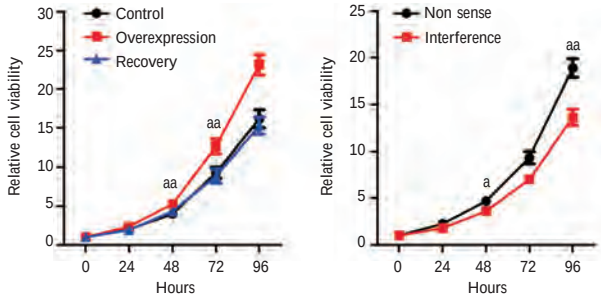
4 ×400

Figure 4 The invasion and migration capabilities of each groups of cells and their comparison crystal violet staining ×400

l ◦◦ ̀Ω ğ 48~96 h ̈E τ

l ◦◦ ̀Ω ğ 48~96 h ̈E

ɟ τ N<0.05 ◆ 5 ɟ

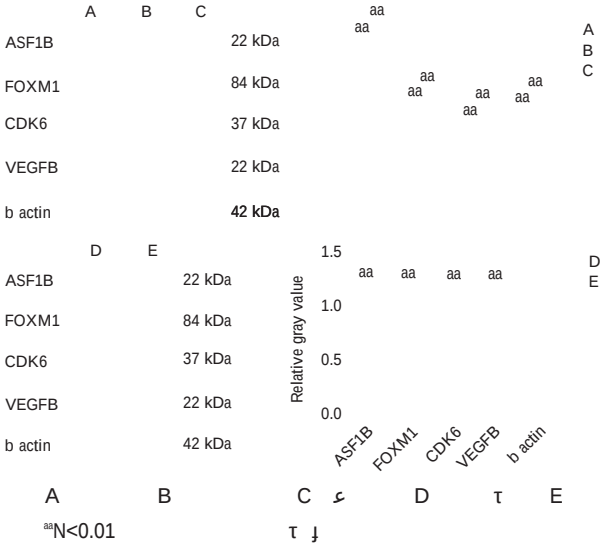


5

Figure 5 The proliferation ability of each groups of cells and their comparison

2.6 ˘ ASF1B ɷFOXM1 ɷCDK6 ẇ VEGFB ẇ ę

ASF1B ɷFOXM1 ɷCDK6 ẇ VEGFB ę Ɦ ɤ FOXM1 ɷCDK6 ẇ VEGFB ę ɳ Ɦ FOXM1 ɷCDK6 ẇ VEGFB ę ɳ Ɦ τ ɟ τ N<0.05 ◆ 6 ɟ



A B C ɤ D τ E

aaN<0.01 τ ɟ

6 ASF1B FOXM1 CDK6 VEGFB

Figure 6 The protein level of ASF1B FOXM1 CDK6 and VEGFB in each groups of cells and their comparison

2.7 ˘ FOXM1 ɷCDK6 ẇ VEGFB ɲ ɣ ˜

FOXM1 ɷCDK6 ẇ VEGFB mRNA Ɦ ɤ FOXM1 ɷCDK6 ẇ VEGFB mRNA ę ɳ Ɦ τ N<0.05 3 FOXM1 ɷCDK6 ẇ VEGFB mRNA ę ɳ Ɦ τ τ N< 0.05 4 ɟ

3 HEC 151 FOXM1 CDK6 VEGFB

Table 3 Gene expression levels of FOXM1 CDK6 and VEGFB in HEC 151 cells

ŏ	FOXM1	CDK6	VEGFB
	1.00±0.07	1.00±0.10	1.00±0.12
	3.12±0.33	2.59±0.12	2.35±0.21
ɤ	1.11±0.12	0.80±0.11	0.75±0.16
D e	11.75	7.92	7.26
N e	<0.05	<0.05	<0.05

4 KLE FOXM1 CDK6 VEGFB

Table 4 Gene expression levels of FOXM1 CDK6 and VEGFB in KLE cells

ŏ	FOXM1	CDK6	VEGFB
τ	1.00±0.09	1.00±0.07	1.00±0.09
	0.19±0.02	0.26±0.04	0.35±0.04
r e	24.80	16.23	8.95
N e	<0.05	<0.05	<0.05

3

' 1 ASF1 Ə ε H3/H4 ɣ˜ ƚ Ά ŏ Ψ ◦◦ Ά ̓Y Ą̈ [7] ɟ ̓O ASF1B ' ˛ ◦◦ Ά Ά AKT/P70 S6K1 ̓Y Ą̈ [6] ; ASF1B ' ̈Ą PI3K/AKT ъ ɛ̈ H [5] ASF1B ≀ H3.3A ў Ə ' ṇ ◦◦ [8] ɟ ɣ ASF1B ' Ə ε ğ ƚ Ά ◻ ◻ ɟ ѽ ɱ ◻ ASF1B Ά ◘ ◻ ɣ FOXM1 ğ Ỉ Ψ Ą̈ FOXM1 ◻ ≀ Ą̈ ɣ [9] ; FOXM1 ' ɳ [10] ɟ ASF1B ' FOXM1 ğ Ỉ Ψ ◻ Ə ɟ ą̊ ASF1B ğ Ỉ Ψ ' ɵ e ɱ ẇ í ◻ ASF1B ğ Ỉ Ψ ̓Y Ά

í ŭ ɐ ẇ ~ ‴ Ặ
ASF1B ’ ㄴ Ά Ỉ ה ה ɻ
ɱ ŭ ᗡ ﻍ غ FOXM1 Ά
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CD56

CD56 Ā † PTC í Ą̈ Ẇ ɵ
e ɟ 2014 1 2015 3 ğ ɔ ˈY PTC 184 ɂ Ə ɛ PTC
ğ ɔ ˈY 78 ɂ Ə ɛ CD56 ɟ PTC
Ỹ Kaplan Meier ŏ CD56 ɵ e COX
ی ŏ Ï̈ ɛ ɟ PTC PTC Ψ CD56 ɳ Ь
τ N<0.05 TNM ŏ ~ ɓ ɓ Ƀ PTC Ψ CD56 ɳ
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ŏ CD56 PTC Ь CD56 PTC τ N<
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PTC Ψ CD56 ā Ā ɔ ɓ ก ˈY Ą̈ ɟ
† CD56 Ï̈ ɛ

XU Chao SHENG Yiquan GE Liwei SHEN Haiying
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ABSTRACT Objective To investigate the relationship between the expression of CD56 and the clinicopathological features of thyroid papillary carcinoma PTC and its predictive value for distant metastasis. Methods From January 2014 to March 2015 184 PTC patients who underwent surgical resection in our hospital were selected as the PTC group while 78 nodular goiter patients who underwent surgical resection in our hospital at the same time were selected as the control group Ж50 anB c as v ɔ ȳ ᴅ meta tasis.

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metastasis and capsule invasion were the influencing factors for the survival without distant metastasis of PTC patients. Conclusion The increase of CD56 expression in PTC is closely related to the deterioration of pathological characteristics and the occurrence of distant metastasis.

KEY WORDS Papillary thyroid carcinoma CD56 Distant metastasis Prediction Influencing factors

í ę Ψ

† papillary thyroid carcinoma PTC

ε ɞ ▌ 70%~80% ɟ PTC Ė

10 ğ 90% ɯ ɔ [1 2] ɟ

ж PTC Ό [3]

PTC ●

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Thyroid Stimulating Hormone TSH

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PTC ŏ PTC Ė [m] ɵ [e] ŏ

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2014 1 2015 3 ğ

ɔ ՝Y PTC 184 ҷ Ə ε PTC Ƀ

71 ҷ ɞ 113 ҷ 37~61 ɞ ը 45.28±

8.28 Ɗ ҁ̓ ğ ɔ ՝Y

78 ҷ Ə ε ę Ψ 31 ҷ ɞ

47 ҷ 33~58 ɞ ը 43.49±9.58 ը

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τ N<0.05 ’ ɟ

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1.2.1 CD56

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2.1 PTC Ά Ψ CD56

PTC PTC Ψ CD56 24 ҷ

13.04% Ψ

CD56 71 ҷ 91.03% ɟ PTC PTC

CD56 ң Њ

τ N<0.05 ɟ ъ 1 ɟ

PTC

1 PTC CD56

SP ×200

Figure 1 Typical CD56 immunohistochemistry of PTC and nodular goiter SP ×200

2.2 ‴ í PTC Ψ CD56

CD56 ğ‴ ʁ ą ʁ ʁ

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ʁ Þ PTC τ

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1 PTC CD56

I %

Table 1 Comparison of CD56 expression in PTC with different clinicopathological features I %

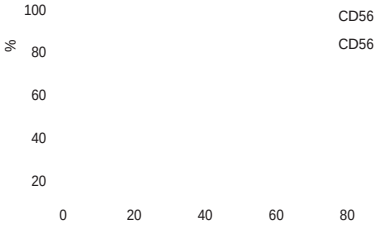
í	ŏ	I	CD56		c^2 e	N e
ą		71	11	15.49	0.612	0.434
		113	13	11.50		
	<45	95	11	11.58	0.371	0.542
	45	89	13	14.61		
	<1 cm	115	12	10.43	1.840	0.175
	1 cm	69	12	17.39		
	₸ ה	117	14	11.97	0.320	0.566
	ה	67	10	14.93		
TNM ŏ	~	120	20	16.67	3.993	0.046
	~	64	4	6.25		
	ı	98	19	19.39	7.441	0.006
		86	5	5.81		
Þ ˬ	ı	103	18	17.48	4.502	0.044
		81	6	7.41		

2.3 CD56 Ά

Kaplan Meier ŏ CD56 PCT

Ң CD56

† τ N<0.05 ɟ ћ 2 ɟ



2 CD56

Kaplan Meier

Figure 2 Kaplan Meier curve of distant metastasis free survival in patients with CD56 positive and negative expression

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2 PTC COX

Table 2 Cox univariate analysis of influencing factors of distant metastasis free survival in PTC patients

ė	Q,C,	PP	73#AG	c^2 e	N e
ą	0.172	0.924	0.551~2.383	0.894	0.325
	0.084	1.089	0.614~2.559	1.039	0.285
	-0.295	0.773	0.504~0.935	5.571	0.020
	-0.271	0.823	0.523~0.946	4.585	0.025
TNM ŏ	-0.347	0.737	0.495~0.914	6.029	0.014
	-0.585	0.709	0.459~0.887	8.684	0.003
Þ ˬ	-0.214	0.842	0.571~0.958	4.283	0.034
CD56	0.384	1.334	1.093~2.958	7.182	0.007

2.5 PTC ĭ ė ė

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COX ع ŏ CD56 ʁ ɶÞ

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3 PTC

Table 3 Cox multivariate analysis of influencing factors of distant metastasis free survival in PTC patients

ė	Q,C,	PP	73#AG	c^2 e	N e
	-0.109	0.834	0.579~1.535	1.371	0.185
	-0.093	0.898	0.523~0.946	4.585	0.025
TNM ŏ	-0.347	0.737	0.495~0.914	6.029	0.014
	-0.585	0.709	0.459~0.887	8.684	0.003
Þ ˬ	-0.214	0.842	0.571~0.958	4.283	0.034
CD56	0.384	1.334	1.093~2.958	7.182	0.007

3

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CD56 ӧ Ψ [m]

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PTC Ψ CD56 ה PTC

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CD56 ң Á PTC ה ׳Y Ă ɟ

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CD56 ’ TNM ŏ ѽ ɞ

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HIF 1 VEGF TIMP

ė 1 HIF 1 ɞ Ǐ ė VEGF ẇ
ΫẠḤ TIMP Ά ˜ ה ♥ ̀Ω Ϗ Ặ ɟ ϥ 2019 2 2020 1
ICU 161 ϛ ˜ Ə ε ɟ ι ה ♥ ̀Ω Ϗ ŏ ε
ה ♥ ̀Ω Ϗ 54 33.54% ẉ ẇ ה ♥ ̀Ω Ϗ ה 107 66.46% ɟ HIF 1 ɞ
VEGF ɞTIMP ẇ Ά ♥ ̀Ω Ϗ ŏ Ặ HIF 1 ɞVEGF ẇ TIMP ╥ ∤ ´
˜ ♥ ̀Ω Ϗ ɞ ɞΆ ɟ ה ♥ ̀Ω Ϗ HIF 1 ɞVEGF ẇ TIMP
ℭ Ћ ה ♥ ̀Ω Ϗ Ė τ N<0.05 1 ɞ2 ♥ ̀Ω Ϗ HIF 1 ɞVEGF ẇ
TIMP Ћ 3 ɞ4 Ė τ N<0.05 ŏ Ϗ O ę HIF 1 ɞVEGF ẇ
TIMP ɔ ė Ά ♥ ̀Ω Ϗ ŏ ∀ Ặ N<0.05 HIF 1 ɞVEGF ẇ
TIMP ´ ˜ ♥ ̀Ω Ϗ ɞ ẇ Ά Ћ ╥m ɟ HIF 1 ɞ
VEGF ẇ TIMP Ά ˜ ה ♥ ̀Ω Ϗ Ė m Ặ ɔ ė ´ ’
♥ ̀Ω Ϗ ɟ
ė 1 Ǐ ė ΫẠḤ ♥ ̀Ω Ϗ

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ABSTRACT Objective To study the correlation between hypoxia inducible factor 1 HIF 1 vascular endothelial growth factor VEGF and tissue inhibitor of matrix metalloproteinases TIMP and pressure injury after heart valve replacement. Methods 161 patients after heart valve replacement in our hospital from February 2019 to January 2020 were selected. The levels of HIF 1 VEGF TIMP and their correlation with the stage of pressure injury were compared in different patients. The sensitivity specificity and accuracy of HIF 1 VEGF and TIMP alone and combined detection for the prediction of postoperative

♥ ̀Ω Ϗ ה ǧ ǧ ; 107 66.46% ה ♥ ̀Ω Ϗ ĥ ◕◕ ♥
Ϗ ’ ε ≀ ≀ Ж 2016 ♥ ̀Ω Ϗ τ ≀ ŏ
’ ¥ [1] ɟ ♥ ̀Ω Ϗ ˝ c Ж◕◕ ĥ [6] ŏ 1 ̀O
Ж ƒ ẹ O ’ ♥ ˝ Ь 2 ’ ŏ
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● ϐ ↄ ẇ ▪ D ė ã̂ ẇ ɟ
˜ ה ♥ ̀Ω Ϗ Ấ Ã 18 ǫ̈ ˝ ί
2~3 ʁ [2] ɟ ė 1 hypoxia induc M
ible factor 1 HIF 1 Ə ε[m] ė ’ ˊ ẹ ђ ɮ ɟ Ã ˝ ŧ
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ė vascular endothelial growth factor ɟ
VEGF [m] Ỉ ≀ 1.2
[3] ’ Ж ǧ’ ‘ ˜ ɤ ṅ Θ0 Θ Ж ̆ ˘ ط ف ˝ _ ج ¥ ف ẓ
Ψ ɟ Ά Ḥ tissue in / /
hibitor of matrix metalloproteinases TIMP [m]
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I [4] ɟ HIF 1 ϐ
VEGF ẇ TIMP Ά ♥ ̀Ω Ϗ ʹY Ă [5] ɟ
HIF 1 ϐVEGF ẇ TIMP Ά
˜ ה ♥ ̀Ω Ϗ Ă w ε ɳ
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ך 2019 2 2020 1 ICU
161 ʔ ˜ Ə ε ɟ
ẹ Ψ 110 ʔ 51 ʔ ◕◕ 47.54±
10.66 ɟ ı ה ♥ ̀Ω Ϗ ŏ ε ה ♥
̀Ω Ϗ 54 33.54% w ẇ ה ♥ ̀Ω Ϗ

Ą ŏ w N<0.05 ε Ė τ ɟ ₰ 1B 3 13 ʀ ₰ 1C 4 5 ʀ ₰ 1D ɟ

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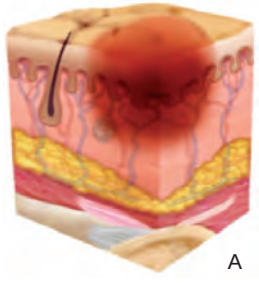
2.1 ♥ ̀Ω Ϗ Ỹ

♥ ̀Ω Ϗ ŏ 1 14 ʀ ₰ 1A 2 22 ʀ



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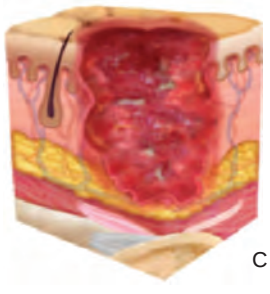

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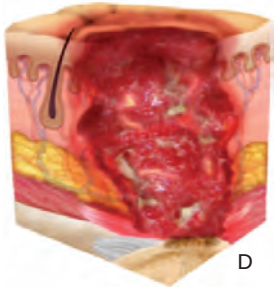

C D

A ε 1 ♥ ̀Ω Ϗ ὰ B ε 2 ♥ ̀Ω Ϗ ŏ C ε 3 ♥ ̀Ω Ϗ ã D ε 4 ♥ ̀Ω Ϗ ὰ ɞ ɟ

1

Figure 1 Image of pressure damage

1 HIF 1 VEGF TIMP $\bar{x}\pm s$

Table 1 Comparison of HIF 1 VEGF and TIMP levels in 2 groups $\bar{x}\pm s$

ᾳ̈	l	HIF 1 ng/L	VEGF ng/L	TIMP g/L
ה	54	3.15±1.98	8.11±2.65	55.29±8.46
ה	107	1.64±0.34	3.55±1.63	33.54±6.55
r e		7.690	13.471	17.990
N e		0.001	0.001	0.001

2.3 ŏ ♥ ̀Ω Ϗ HIF 1 ɞVEGF ɞ TIMP

ŏ ♥ ̀Ω Ϗ HIF 1 ɞVEGF ᾐ TIMP 4 >3 >2 >1 Ė τ N<0.05 2 ɟ

2 HIF 1 VEGF TIMP $\bar{x}\pm s$

Table 2 Comparison of HIF 1 VEGF and TIMP levels in patients with different stages of pressure injury $\bar{x}\pm s$

ᾳ̈	l	HIF 1 ng/L	VEGF ng/L	TIMP g/L
1	14	1.74±0.41	4.41±1.05	35.32±5.17
2	22	1.97±0.52	5.13±2.64	37.51±5.82
3	13	2.96±1.01	7.15±2.66	52.64±6.24
4	5	3.08±1.25	8.29±2.93	54.69±7.53
D e		8.94	5.44	31.79
N e		0.001	0.003	0.001

2.4 HIF 1 ɞVEGF ᾐ TIMP ~ ♥ ̀Ω Ϗ

HIF 1 ɞVEGF ᾐ TIMP ´ ~ ♥ ̀Ω Ϗ ɞ ᾐ Ἀ Ь ╥m

2.2 Ξ HIF 1 ɞVEGF ᾐ TIMP

ה ♥ ̀Ω Ϗ HIF 1 ɞVEGF ᾐ TIMP ᾠ Ь ה ♥ ̀Ω Ϗ Ė τ N<0.05 1 ɟ

HIF 1 ɞVEGF ᾐ TIMP ɟ 3 ɟ

3 HIF 1 VEGF TIMP

Table 34 Sensitivity specificity and accuracy of HIF 1 VEGF and TIMP in predicting postoperative pressure injury

	ᾳ̈	í ʀ		Ἀ		
		ה	ה	%	%	%
HIF 1	ה	38	19	70.37	82.24	78.26
	ה	16	88			
VEGF	ה	37	22	68.52	79.44	75.78
	ה	17	85			
TIMP	ה	36	23	66.67	78.50	74.53
	ה	18	84			
ɞ ´	ה	48	10	88.89	90.64	90.06
	ה	6	97			

2.5 HIF 1 ɞVEGF ᾐ TIMP Ά ♥ ̀Ω Ϗ ŏ Ą ŏ

♥ ̀Ω Ϗ ŏ Ά HIF 1 p ; 0.564 N ; 0.003 ɞVEGF p ; 0.432 N ; 0.024 ᾐ TIMP p ; 0.506 N ; 0.012 ∀ Ą ɟ

3

♥ ̀Ω Ϗ í ~ ε m ה Ϛ ã ├ ► í ∤ ├ ж ∤ ₰ ’ m ĭ Ж ₰ ᾐ ̓ Ж H ₰ [7] ɟ ה ♥ ̀Ω Ϗ H 4 ʁ [8] ɟ ᾠ

Ặ ♥ ̀Ω Ҡ ה Ӛ ę ה
Ӛ ặ ң ~ ה ♥
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VEGF ẇ ε ė Chloe [9]
VEGF ל Ά Ђ
ɞҠ i ´ ɞw ẇ w ‴ ɞ ɞ ה
ɟ ѽ ε VEGF ’ [m] Y
Ӛ ገ Ңᵐ ገ ė ‴
c c‾ ˅ Ң Ő [10] ɟ Fan [11] ה
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ɟ Ң [12] ̀O ♥ ̀Ω Ҡ
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VEGF ╗ ɟ
HIF 1 Ңᵐ ė Ң
Ỹ ˘ ė Ű ς
F G D

SD/CRL HCG E2 IVF/ICSI ET

ш / SD/CRL e ´ ж
HCG ɵ J E2 l ɔ / ◓ Ì ╥ IVF/ICSI ET У
ɵ e ɟ 328 Y IVF/ICSI ET ٩ ŭ У Ά У
HCG ŒE2 ŒSD/CRL e ѡ ‟ ’ í У Ï ė ŭ SD/CRL ´
HCG ŒE2 У ɵ e ɟ У HCG ŒE2 ҥ Ҥ У
Ė τ N<0.05 SD/CRL e Ҥ У Ė τ N<
0.05 >35 У Ҥ 30~35 Ά <30 ΄Y 30~35 Ҥ<30 Ė
τ N<0.05 ŒSD/CRL e Ҥ У ● ė N<0.05 ˜ 14 d
HCG ŒE2 ε У ٦ ė N<0.05 E2 У 81.7% 71.5% HCG
82.8% 79.3% SD/CRL 86.9% 73.1% ɕ ´ 91.7% 89.2% ɟ
SD/CRL e ´ HCG ŒE2 ’ ε IVF/ICSI ET У w ˚ í Ə
Ė τ ɟ
ш / ж J l ɔ / ◓ Ì ╥

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ABSTRACT Objective To observe the predictive value of gestational sac diameter/crown rump length SD/CRL ratio combined with serum human chorionic gonadotropin HCG and estradiol E2 levels in early abortion of patients undergoing in vitro fertilization/intracytoplasmic sperm injection embryo transfer IVF/ICSI ET . Methods A retrospective analysis was performed among 328 patients receiving IVF/ ICSI ET in the hospital. The levels of serum HCG and E2 SD/CRL ratio and clinical data were compared between the early abortion group and the non early abortion group. Influencing factors of early abortion were analyzed. The predictive value of SD/CRL ratio combined with serum HCG and E2 levels for early abortion was discussed. Results Theserum HCG and E2 levels of the early abortion group were significantly lower than those of the non early abortion group N<0.05 while SD/CRL ratio was significantly higher than that of

the non early abortion group N<0.05 . The early abortion rate in >35 years old group was significantly higher than that in 30~35 years old and <30 years old groups and the 30~ 35 years old group was significantly higher than those under 30 years old group N<0.05 . Age and SD/CRL ratio were independent risk factors for early abortion N<0.05 while serum HCG and E2 at 14d after transplantation are protective factors N<0.05 . The sensitivity and specificity of E2 HCG SD/CRL ratio and their combination for predicting early abortion were 81.7% 71.5% 82.8% 79.3% 86.9% 73.1% and 91.7% 89.2% respectively. Conclusion The SD/CRL ratio combined with serum HCG and E2 can provide an important basis for the prediction of early abortion of patients undergoing IVF/ICSI ET which is of great significance for clinical practice.

KEY WORDS Gestational sac diameter/crown rump length human chorionic gonadotropin Estradiol In vitro fertilization/intracytoplasmic sperm injection embryo transfer

ğĭ ѧ J ãã ;
ğĭ ̋ Ψ ą̈ ɟ
l ɔ /◓ Ỉ ╥

in vitro fertilization/Intracytoplasmic sperm injection embryo transfer IVF/ICSI ET ѡ 15%~20% í ą̈ Ъ 40%~50% ╥ У ¯ 35% ˆ У ˇΩ ң 25% ΄Y 12 ٧ ѽ У 27% Ъ [1 2] ɟ ˇA IVF/ICSI ET У í Ė τ ɟ ѡ ж ˛ beta human chorionic gonadotrophin HCG ɵ J estradiol E2 Ė [m] ɵ [e 3] ɟ ğĭ IVF/ICSI ET ˜ У Ą Ψ HCG ΄Y ę[m] ٧ ę ƀ ´ У ѡ ẇ Ң Нь У ѽ ζ [4] ɟ J ɕ Нь У ж Ą Нь ę У У Ą ɟ ζ ш / sac diameter/crown rump length SD/CRL [e] ´ HCG ɶE2 IVF/ICSI ET У ɵ [e] ɟ

1

1.1 [m]

ٹ 2018 1 2019 2 ٹ ѓ 328 ѯ IVF/ICSI ET ٧ ɟ 25~42 ҕ 33.46±6.01 ɟ 328 ѯ ı ѣ У ŏ ε У l=64 Ά У l=264 ɟ

Ấ ˇA ɔ IVF/ICSI ET ΄Y ε ╥ í Ė ˋΩ Ά ˋΩ ˛ Ш ɟ ˇA ╥ ´ ◓ Нў Ɑ ẹ ◓ ị́ ´ ̋ ̋ ٹ ɟ ´ ├ Ң ٧ Ж Ą̆ ɟ

1.2

IVF/ICSI ET ğĭ ˜ 30 d Є ѡ XARIO SSA 660A ىي Ѧ Z ãã Ỉ Ỹ PVT 661VT 6MHZ SD ɶCRL ɵ ◓ ш ҕ yolk sac diameter YSD ɵ heart rate HR ٹ Ң ę Ψ CRL [e] Ψ ΄Y ę ą̈ φ SD [e] ε + /2 ɟ ˜ ŏ ѡ ŏ ẍ ˜ 14 d HCG Ά E2 Ѧ ƀ ε DNM 9606 ىي Ѧ ├ ƀ ắ ˘ ɟ

1.3 У ó [5]

˜ 14 d HCG 5 IU/L ˜ 30 d Ỉ ж 13 ٧ ˜ 14 d HCG 5 IU/L ѣ ж ж ğĭ 12 ٧ Ỉ ɟ

1.4

У Ά У HCG ɶE2 ɶSD/CRL [e] ̋ ̋ ˆ í ɵ l body Mass Index BMI ɵ ̋ У ĭ ẹ ŏ ŏ SD/CRL ´ HCG ɶE2 У ɵ [e] ɟ ę Ψ HCG ɶE2 ɶSD/CRL ŏ ą̈ ѡ IVF/ICSI ET Ψ Ң ε ŏ ɟ

1.5

ٹ SPSS 19.0 Θ ѡ l % ƒ c^2 ѡ $\bar{x} \pm s$

ƒ r ˥ COX ٮ ŏ Є w ĭ ė ŏ w ɔ Ə ROC У ɵ e ŏ ɟ w N<0.05 ε τ ɟ

2

2.1 Ξ HCG ɶE2 ɶSD/CRL e

У HCG ɶE2 ҥ Ҍ У Ė τ N<0.05 SD/CRL e Ҍ У Ė τ N<0.05 ɟ 1 ɟ

1 HCG E2 SD/CRL $\bar{x}\pm s$

Table 1 Comparison of serum HCG level E2 level and SD/CRL ratio between 2 groups $\bar{x}\pm s$

ą̈	l	HCG IU/L	E2 pg/mL	SD/CRL e
У	64	1380.18±206.37	260.46±40.95	6.23±8.75
У	264	2305.74±382.95	546.14±42.38	4.06±6.38
r e		18.674	48.694	2.257
N e		<0.001	<0.001	0.025

2.2 ˝ ˀ í Ά HCG ɶE2 ɷ SD/CRL e У

˝ ˀ BMI ɷ ˝ У τ N>0.05 У ğ ɷ HCG ɶE2 ẇ SD/CRL e ɔ Ė τ N<0.05 ɟ 2 ɟ

2.3 COX ٮ ŏ

ɶSD/CRL e У • ė N<0.05 ˜ 14 d HCG ɶE2 ε У ˥ ė N<0.05 ɟ 3 ɟ

2.4 SD/CRL ´ HCG ɶE2 У ɵ e ŏ

У e ε 1 У e ε 0 ł SD/CRL Ńẁ HCG Ńẁ E2 Ń Ấł ƾ Ń ROC ŏ ɟ E2 81.7% 71.5%

2 HCG E2 SD/CRL l %

Table 2 Comparison of early abortion rate among patients with different clinical data different serum HCG levels E2 levels and SD/CRL ratios l %

		l	У	c^2 e	N e
	<30	98	7 7.14	19.465	<0.001
	30~35	110	20 18.18		
	>35	120	37 30.83		
BMI kg/m²	<18.5	52	12 23.08	3.845	0.146
	18.5~24.0	208	34 16.35		
	>24.0	68	18 26.47		
˝	1~5	106	16 15.09	2.658	0.265
	6~10	118	28 23.73		
	>10	104	20 19.23		
HCG IU/L	1800	109	34 31.19	14.182	<0.001
	<1800	219	30 13.70		
E2 pg/mL	400	126	38 30.16	14.766	<0.001
	>400	202	26 12.87		
SD/CRL e	<5	286	34 11.89	82.667	<0.001
	5	42	30 71.43		

HCG 82.8% 79.3% SD/CRL 86.9% 73.1% ی ´ ΆȮ ی ´ ی ɕ ´ 91.7% 89.2% ɟ 4 ɻ ɚ 1 ɟ

4 SD/CRL HCG E2 ROC

Table 4 Areas under ROC curves of SD/CRL ratio combined with serum HCG and E2 levels for prediction of early abortion

ƾ		Ά	95%AĠ	N e
E2	0.762	0.078	0.614~0.935	0.007
HCG	0.771	0.080	0.609~0.942	0.005
SD/CRL	0.794	0.082	0.675~0.951	0.002
ɕ ´	0.825	0.063	0.736~0.982	<0.001

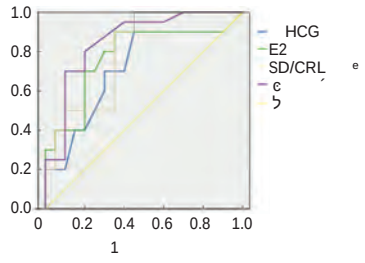
3

HCG ε Ψ Ế У ę ζ ɻ Ж ۼ Ă ɵ ´ Ҍ HCG ė í

3 COX

Table 3 COX regression analysis of influencing factors of early abortion

ƾ	@ e	Q,C, e	U_jb e	Cvn @ e	95%AĠ	N e
	6.043	3.785	6.402	2.736	1.650~3.879	<0.001
HCG	0.734	2.368	4.271	2.062	1.347~3.584	<0.001
E2	0.602	2.258	4.369	2.014	1.286~3.475	<0.001
SD/CRL e	7.453	3.968	7.684	3.065	1.543~5.782	<0.001



1 SD/CRL HCG E2 ROC

Figure 1 ROC curves of SD/CRL ratio combined with serum HCG and E2 levels for prediction of early abortion

HCG ΎA א ж l HCG ɟ IVF/ICSI ET˜ 14 d HCG ΎΩ ę У ң[6] ɟ E2 ε א ◓ ţ ' Ỹ Ǐ ɔ ѡ ѠI ѫ ŏ E2 ' ѡ ϒ◓ ה Ά ˀ ϒ◓ Ė ɔ ΏɟÍ ε ◓ ţ ' ˜E ε Ώ ң Ɑ ė ɟ Ό E2 ; ' ζ ǐ ч 1 interleukin 1 IL 1 в ϣ ė tumor necrosis factor TNF ѡ Ѡ interferon IFN ŏ Ǐ ɔ ǐ[7] ɟ Ą E2 ŏ ; ' Ǐ ɔ Ϗ ъ ѡ Ѡ Í У ǐ[8] ɟ Ψ У HCG Ά E2 ң Ь У Ά [9] m ɟ ė ŏ ה ˜ 14 d HCG ŒE2 ε IVF/ICSI ET˜ У ϒ ė ę ң Ά У ğ ɟ Ь Ψ ą̃ ɟ Ό У ╗ ∤ в l Ά в в ▪ в ш в в◓ ш Ą̃[10 11] ɟ SD ŒCRL ŒHR ŒYSD Ђ ה ę ε ὰ ğ Ψ ה ˝ ' ц Ə ɟ ą̃ CRL Í e ε 4 mm 5 mm У 8.3% Í e 5.3 mm ˚ ε 0.0%[12] ɟ Rodgers[13] ה CRL Ь 7 mm ΄Y ˚ ε 0.0% MSD Ь 25 mm ΄Y ą̃ ˚ ε 0.0% CRL Ά MSD ' Ь У ɟ IVF/ICSI ET˜ У SD/CRL e ╗ ę Ά У Ą̃ ΄Y Ά ɔ m ɟ ѫ ◓ ţ ' ˜E ˜E ŏ Ό l ˝ ŏ ė Ь l ζ ● ė[14] ɟ Ψ Ế trophoblast TE ה ϟ ε ˀ ŏ HCG l ' ɟ TE ѫ ѳŏ ɔ HCG ŏ ˝ ה ˝ [15] ɟ T ´ HCG Ά MSD/CRL IVF/ICSI ET Ė . Ɓ ę ´ 87.57%[16] ɟ ὰ E2 в HCG ŒSD/CRL ´ ѳ e ROC ŏ ה З ϑ У Ė m ѳ e ΄Y ε ´ ѳ e ˘ ╥ ɟ ɔ SD/CRL e ´ HCG ŒE2 IVF/ICSI ET˜ У Ė ѳ e ɟ

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miR 4262 A549

; miR 4262 A549 ΐ ϣ ΅Ạ ɟ qRT PCR
Ψ miR 4262 ƚ ɔ ɟ ǵ A549 Ψ miR 4262 inhibitor MTT ɯ
Ὼ Transwell ˬ ɻ Ὼ Western blot E cadherin ɷvimentin ɟ ɱ
Ɵ miR 4262 ɻ KLF3 3 UTR ´ Ɦ ẉ ˜ Ă ɟ qRT PCR
Ψ KLF3 mRNA ƚ ɔ ŏ ę Ά miR 4262 Ặ ɟ ǵ A549 Ψ
miR 4262 inhibitor ɷKLF3 siRNA ɯ ę ɷ ƚ ɔ ɟ A549 Ψ miR 4262
₹ ɟ miR 4262 inhibitor ˜ A549 ɯ ę ɻ Ὼ ɦ Ψ
E cadherin ₹ vimentin ; ɟ miR 4262 Ά KLF3 ˜ Ặ ɟ ;
miR 4262 ɜ A549 Ψ KLF3 ɟ KLF3 siRNA ' ẉ miR 4262 inhibitor A549
ɯ ę ɻ ΅Ạ ' ɟ ; miR 4262 ΅Ạ A549 Ə ΅Ạ Ά ˜ ɜ
KLF3 Ặ ɟ
KLF3 miR 4262

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ABSTRACT Objective To explore the effect and mechanism of down regulation of miR 4262 on the metastatic potential of lung cancer cell A549. Methods qRT PCR was used to detect miR 4262 expression in lung cancer cells. Lung cancer cell A549 were transfected with miR 4262 inhibitor MTT was used to measure proliferation transwell cells were used to measure invasion and migration and western blot analysis was used to measure E cadherin and vimentin protein expression. Bioinformatics software predicts that miR 4262 and KLF3 have binding sites at the 3 UTR end and the luciferase system identifies the targeting relationship. qRT PCR was used to detect changes in the expression of KLF3 mRNA in lung cancer tissues and to analyze the correlation between its expression level and miR 4262. Lung cancer cells A549 were transfected with miR 4262 inhibitor and KLF3 siRNA to detect cell proliferation invasion and migration changes. Results The expression level of miR 4262 was increased in lung cancer tissues and lung cancer cells. After transfection with miR 4262 inhibitor lung cancer cell A549 had reduced proliferation invasion and migration ability and the expression level of E cadherin protein in the cells increased while the level of vimentin decreased. Down regulation of miR 4262 up regulated the expression of KLF3 in lung cancer cell A549. KLF3 siRNA can reverse the inhibitory function of miR 4262 inhibitor on the proliferation invasion and migration of lung cancer cell A549. Conclusion Down regulation of miR 4262 inhibits the metastatic potential of lung cancer cell A549 and the mechanism of action is related to the targeted up regulation of KLF3 expression.

KEY WORDS Lung cancer KLF3 miR 4262 Migration

Ė í ‴ в
ğ ה Ъ
΄Y Нь [1] ɟ ˬ
в ۱ ɔ ɔ epithelial mesenchymal
transition EMT Ὼ Ά
Ặ ң в Ἄ ۱
ᾥ ɟ RNA microR
NA miRNA [m] Y ж l Ỉ
RNA ŏ Ė Ə в
ה в ה вẍ miRNA
Ἄ ĭ ۷ [2] ɟ ж Ⱨ miRNA
‴ Ấ ה ה Ά miRNA
Ặ ΄Y miRNA ’ в
ŏ [3] ɟ ğ Ψ miRNA ƽ Ά
۱ ŏ ~ miRNA
ε [4] ɟ ᾥ Нь miR 4262 ğ
ˬ в ۱ EMT Ψ Ə ɟ
miR 4262 ĭ
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1

1.1

miRcute ھ ی miRNA cDNA [m] ´
΄Ң вmiRcute ھ ی miRNA ẉ ΄Ң
SYBR Green вQuant one step qRT PCR Kit
SYBR Green ج ɔ ← Ш ắ
˘ vimentin l вKLF3 l ہ Abcam
E cadherin l ۱ HRP J ج ہ
Santa Cruz Biotechnology inhibitor control вmiR 4262
inhibitor ɔ ` Ἄ ắ ˘ WT
ی ۱ MUT ƽ ی ẉ ۷ l `
ɔ ắ ˘ KLF3 siRNA ۱
siRNA control ắ ˘
´ NCI H446 вA549 вNL9980
ہ ATCC ɔ HBE ɔ
╪ ắ ˘ ɟ
1.2 qRT PCR miR 4262 ۱ KLF3 mRNA

ŏ ᾳ Trizol ΄Ң ۷ NCI 466
A549 NL9980 ˀ ۷ NCI H446 в
A549 вNL9980 Ⱡ Ⱬ 0 . ŧ 0 ɒ ک

Ψ ɟ ẉ Ḥ ẉ
ƾ ɔ ɟ ˀ Control ɷAnti NC ɷ
Anti miR 4262 qRT PCR ɻ Western blot
ŏ ą̈ Ψ I JD1 mRNA ɻ ƾ
ɔ ˀ 1.2 ɻ 1.6 ɟ

1.8 KLF3 siRNA ; miR 4262 ˈ
ŏ ą̈ ğ A549 Ψ miR 4262 inhibitor ɷ
siRNA control ɻ miR 4262 inhibitor ɷKLF3 siRNA
Ă ε Anti miR 4262+si NC ɻ Anti miR
4262+si KLF3 ɲ Ē 48h ẅ˜ MTT ɷ
ɷTranswell ˬ ɷWestern blot
E cadherin ɷvimentin ɷKLF3 ɟ

1.9 ŏ
SPSS 21.0 Θ ŏ
x̄±s Ξ φ r
Ŧ Ė ŏ N<0.05 ε
τ ɟ

2

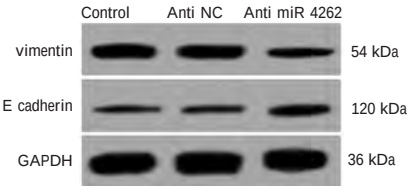
2.1 miR 4262 ğ Ψ
NCI H446 ɷA549 ɷNL9980 Ψ miR
4262 Ҥ ɔ HBE
N : 0.05 ɟ 1 ɟ

1 miR 4262
x̄±s

Table 1 miR 4262 expression levels in lung cancer cells and normal bronchial epithelial cells x̄±s

	miR 4262
HBE	1.00±0.12
NCI H446	1.76±0.13
A549	2.65±0.23
NL9980	2.02±0.15
D e	157.42
N e	<0.001

2.2 ; miR 4262 ɷ ɸ ɷ
ɻ EMT ĭ
miR 4262 inhibitor˜ Ψ miR
4262 ҕ OD e ɸ ɷ
ẉ ẘ Ψ vimentin ɷ ;
E cadherin ₹ N<0.05 ȣ 1 ɻ 2 ɟ



1 Western blot E cadherin vimentin
Figure 1 Western blot method to measure E cadherin and vimentin protein expression

2.3 miR 4262 ɻ KLF3 Ў ε ˜ Ą
ɱ Θ ɲ miR 4262 ɻ KLF3
3′UTR Ў ´ Ҥ ′Y WT KLF3 ɻ miR
4262 inhibitor Ă ˜ ẉ ₹
N<0.05 ȣ 2 ɻ 3 ɟ

2 miR 4262 KLF3 3 UTR
Figure 2 MiR 4262 and KLF3 3 UTR end binding site

3 x̄±s
Table 3 Comparison of cell luciferase activity x̄±s

ą̈	MUT	WT
Anti NC	1.00±0.11	1.00±0.12
Anti miR 426	0.98±0.08	1.45±0.13
r e	0.67	7.63
N e	0.44	<0.001

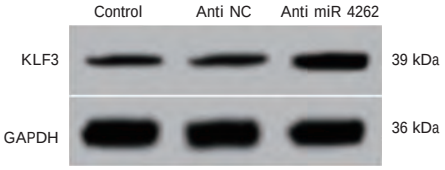
2.4 ; miR 4262 Ψ KLF3 ĭ
miR 4262 inhibitor ˜ Ψ
KLF3 ɻ mRNA ₹ N<0.05 ȣ 3
ɻ 4 ɟ

2.5 KLF3 siRNA ; miR 4262 ̈Ą
ɷ ɸ ɷ ɷEMT ˈ
Ά Ă siRNA control ɻ miR 4262 inhibitor

2 OD E cadherin vimentin x̄±s
Table 2 Lung cancer cell OD value, invasion number, migration number, and E cadherin and vimentin protein levels x̄±s

ą̈	miR 4262	OD e	ˬ		E cadherin	vimentin
Control	1.00±0.09	0.43±0.04	98.45±9.33	125.30±10.35	0.22±0.02	0.56±0.05
Anti NC	0.97±0.12	0.44±0.03	99.24±7.25	126.83±11.20	0.21±0.03	0.54±0.04
Anti miR 42 62	0.45±0.05	0.32±0.02	64.36±4.21	85.34±7.29	0.35±0.05	0.33±0.02
D e	103.29	41.28	68.05	52.30	43.34	97.40
N e	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

Ă KLF3 siRNA ∤ miR 4262 inhibitor ˜ OD e ę в ∤ vimentin ☪ ╗ Ψ KLF3 в E cadherin ң N<0.05 ɟ ♣ 4 ∤ 5 ɟ



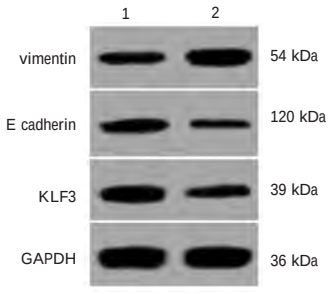
3 Western blot miR 4262 inhibitor KLF3

Figure 3 Western blot detection of KLF3 protein expression in lung cancer cells transfected with miR 4262 inhibitor

4 miR 4262 inhibitor KLF3 mRNA $\bar{x}\pm s$

Table 4 Comparison of KLF3 protein and mRNA levels in lung cancer cells transfected with miR 4262 inhibitor $\bar{x}\pm s$

ą	KLF3	I JD1 mRNA
Control	0.28±0.03	1.00±0.08
Anti NC	0.29±0.05	0.99±0.13
Anti miR 4262	0.67±0.07	2.24±0.21
D e	160.89	207.00
N e	<0.001	<0.001



4 Western blot KLF3 E cadherin vimentin

Figure 4 Western blot detection of KLF3 E cadherin vimentin protein expression levels in transfected cells

3

miRNA ğ ∦ I Ψ ğ Ύ Ė ‖ ŏ ' miRNA Ά ŭ ɔ в ɔ в ☜ Ă ɟ miRNA ' ж ę ' w غ ה Ə ל Ά ą̈ I ų в II вж ' ∦ Ψ [5] ɟ miRNA ל Ά в Ҡ miRNA ĭ ε ה Ə [6] ɟ ☜ ∤ ς ɔ ą̈ miRNA Ə З Ά Ă miRNA ğ Ψ ה Ч غ ג غ Ə ĭ ☜ ∤ [7] ɟ miR 4262 ğ † в Ψ ę ' w ∤ [8] ɟ ğ ɟ Ψ ε miR 4262 ΅Ą ☜ [9] ɟ miR 4262 ' ğ ∤ Ψ ה Ə ɟ ε Ъ Ά ∤ Ὼ Ă w Ά EMT Ύ Ă [10] ɟ EMT ğ Ь I Ĭ ę ğ ה в Ψ Ă ɟ EMT ה ɔ ی ¨E ی ☜ ɟ E cadherin ɔ vimentin [11] ɟ ה EMT ☜ ς EMT ς [12] ɟ ; miR 4262 ˜ Ψ E cadherin ╗ vimentin ң ; miR 4262 ' w ң Ά ∨ ∤ ´ ☪ ; miR 4262 Ė ΅Ą Ə ɟ miRNA Ə ΅Ą Ά ˜ غ ג Ă Ύ miRNA غ ג ' ˀ Y ğ ‴

5 OD KLF3 E cadherin vimentin $\bar{x}\pm s$

Table 5 Lung cancer cell OD value invasion number migration number and KLF3 E cadherin vimentin protein level comparison $\bar{x}\pm s$

ą	OD e	∨		E cadherin	vimentin	KLF3
Anti miR 426 2+si NC	0.33±0.03	65.67±5.75	86.32±5.76	0.39±0.06	0.34±0.04	0.63±0.08
Anti miR 4262+si KLF3	0.42±0.04	86.43±6.87	110.54±9.04	0.23±0.04	0.58±0.07	0.32±0.04
r e	5.40	6.95	6.78	6.67	8.93	10.40
N e	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

ˀ Ψ ɲ ɣ ’ ˠ˃ˀ [13] ɻ
; KLF3 ’ ɯ ; miR 4262
ʍ ɞ ɕ ʅ EMT ΅Ạ Ə
miR 4262 ’ KLF3 ǐ
ʅ ɻ
φ miR 4262 ɷ Ψ ’ ɲ ˛ Ə
; ẹ ’ ɯ ˜ ˛ KLF3 ɳ
ε miR 4262 ɷ Ψ Ə
ɯ Ъ ɔ ε ˜ ɲ ɣ ɯ Ъ ɻ
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IGF 1 IGFBP 3

Hcy

Ẉ ' ‶Ε ң CH ụ ẹ 1 IGF 1 ɞ

ẹ ´ IGFBP 3 ᾔ ﻯ ╚ Hcy ל כ ᾔ ę Ά ה Ặ ɟ ך

2017 7 2020 7 90 ʒ CH ụ í ε ˀ ך 85 ʒ ɾ ụ ε

Ξ ụ ɞl ɞ ɒ Ţ ẹ ה Ỹ ẍ ŭ ɞ ẉ ẍ

Ξ IGF 1 ɗGFBP 3 ᾔ Hcy ŭ ę Ά ה Ặ ɟ Ξ ụ ɗO l ɞ

ɞ ɞ ɞ ɞl BMI ᶍ τ N<0.05 ɟ ụ

ɒ ɞ Ə ɒ ɞ ɒ ң Ь Ė τ N<0.05 ᾧ Ά Ǝ Ψ

ụ Ὸ ң Ь Ė

control group and the level of Hcy was significantly higher than that of the control group and the difference was statistically significant N : 0.05 . Conclusions The levels of IGF 1 IGFBP 3 and Hcy have a certain correlation with children s IQ height and weight. Children with CH can return to normal levels after early diagnosis and treatment.

KEY WORDS Congenital hypothyroidism Insulin like growth factor binding protein Insulin like growth factor 1 Homocysteine

Ẉ ' ‶E ҥ congenital hypothyroidism CH Ҍ ´ ѡ ŏ ‴ ѡ ц ҥ ; ɞl ۱ ה ε ζ m [1] ɟ CH ṿ Ỉ ŏ φ m ɟ ṿ Ҍ ï ė ىي í ȳ ṿ l ɞ Ὼ ה Ὸ [2] ɟ í ɔ ζ ε ṿ ɞ Ὼ ה ~ ṿ O ĭ ɟ ; B ė ж l Ə ' Ȧ ẹ Ặ ‘Y [3] ɟ ̃ ىي ╚ homocysteine Hcy ц У m ‶ ﻧ ﻭ Ỉ ﻧ ɟ Hcy ├ ε ė ɟ ' ҥ ; ц Ж ã Y ɔ ' ⷮ [4] ɟ CH ṿ ė 1 Insulin like growth factor IGF 1 ɞ ė ´ 3 Insulin like growth factor binding protein IGFBP 3 ѡ Hcy ŏ ẹ ƚ ɔ ѡ Ȧ CH ṿ ה Ặ ɟ

1

1.1 m

ך 2017 7 2020 7 90 ϗ CH ṿ Ẩ ẹ Ψ 34 ϗ 56 ϗ ⷮ 5.11±2.17 ɟ ך ̃ 85 ϗ ⊬ ṿ Ə ε ẹ Ψ 31 ϗ 54 ϗ ⷮ 4.74±1.58 ɟ Ẩ ‶A ṿ ⷮ í ε CH serum free T4 FT_4 ҥ ҥ Ҍ e ę thyroid stimulating hormone TSH ﷺ 20 mU/L ϗ ´ ẹ ђ Ỉ ŏ ‶A í M ´ У ɞO ṿ ´ ṿ ´ ´ ɞ ζ ɔ Ẉ ɟ Ξ m τ Ė ' N<0.05 ɟ ├ Ң ۱ Ж ‶A ɔ ̃ Ш ɟ

1.2

1.2.1 ṿ

ṿ ~ i ẋ ‴Ạ ắ ˘ ۵ ‶A J20160065 ṿ í Ỹ ѡ ' ɟ TSH م ̃ FT_4 ﷺ ۰ م ɟ

1.2.2 IGF 1 ɗGFBP 3 ѡ Hcy

ⷮ ﷺ ɔ ך 6 mL ◗ Ẩ ‶H'Ң ŏ Ψ 400 r/min ŏ Ὸ ~ ҥ ך Ψ ɟ IGF 1 ɞ IGFBP 3 ẍ ŏ Ⱥ ɔ ´ ғ ắ ˘ У Ң IGF 1 Ң ‶A ˝ ۵ 20142405760 IGFBP 3 Ң ‶A ˝ ۵ 20162404085 ε ← Ш ← w ɟ Hcy ɔ ẉ ۰ ẍ Ⱥ ɔ ﻧ ắ ˘ AbbotIMx ẍ ŏ Ⱥ Ң Hcy Ң ‶A ˝ ‶A 2011 2400126 ˝ ﻁ ẋ ắ ˘ w ɟ Ė l Ə O Ш ‘Y ⷮ m ẍ א ă ɟ

1.3

ŏ Ξ ṿ ה Ỹ ɞ Ὼ Ỹ Ξ ṿ IGF 1 ɗGFBP 3 ѡ Hcy ƚ ɔ Ỹ ŏ ɔ ė ƚ ɔ Ȧ CH ṿ l ה ɞ Ὼ ה Ặ ɟ ה Ȧ ‴Ạ ה Ỹ ħ Ψ ۵ 7 w ; ṿ ה ל ‶A ђ [5] Ţ Ƥ ṿ ɞl ѡ ẹ ‶A ŏ standard deviation scoring SDS ɞ l body mass index BMI ɟ Ὼ ll Ψ ۵ ṿ Ὼ Chinese Wechsler Young Children scale of Intelli

gence C WYCSI [6] ۱ Ə

ɟ Ţ ɒ <70 ŏ ε Ὼ ɳ

; 90 ŏ ε ɟ ᶐ ˀ m ˜ Ό Δ ᷉ Ό

ж ɟ

1.4

SPSS 20.0 Θ ŏ

w x̄±s Ξ r w

l % c^2 Ặ ʄ Nc_pqml Ặ

ŏ ώ ɾ ŏ N<0.05 ε

τ ɟ

2

2.1 Ξ ỵ ה Ỹ

Ξ ỵ ה Ỹ

τ N<0.05 1 ɟ

2.2 Ξ ỵ Ὼ Ỹ

ỵ ɒ ɐ Ə ɒ ɐ ɒ ɐ

Ά Ǝ Ψ ɳ Ь Ė

τ N : 0.05 ж Ξ ẇ Ə

τ N<0.05 2 ɟ

1 x̄±s

Table 1 Comparison of children s growth and development between the two groups x̄±s

		l=90	l=85	r e	N e
		5.11±2.17	4.74±1.58	1.283	0.201
Ό l g		3486.97±487.77	3403.11±392.67	1.248	0.214
Ю		25.82±3.81	25.49±1.75	0.729	0.467
		7.14±1.66	7.06±1.75	0.310	0.757
		12.62±1.54	12.41±1.32	0.966	0.335
		7.45±2.31	6.84±2.01	1.859	0.065
l	SDS	0.52±0.65	0.83±1.47	1.821	0.070
	SDS	0.57±0.81	0.55±0.97	0.148	0.882
BMI	kg/m^2	14.90±1.06	15.21±1.66	1.481	0.141

2 x̄±s

Table 2 Comparison of intelligence between the two groups x̄±s

᷉	l	ɒ		Ə ɒ	Ə	ɒ		Ǝ
	90	88.26±12.41	18.37±3.12	103.77±12.43	19.32±3.17	95.05±11.32	4.67±1.31	1.04±1.14
	85	109.03±12.85	19.12±2.45	112.90±9.75	20.12±3.01	111.27±10.66	5.89±1.04	2.32±1.17
r e		10.877	1.762	5.385	1.710	9.745	6.798	7.329
N e		0.001	0.080	0.001	0.089	0.001	0.001	0.001

2.3 Ξ ỵ IGF 1 ȣGFBP 3 ẇ Hcy

IGF 1 ȣGFBP 3 ɳ Ь

Hcy Ь ᶐ Ė τ

N<0.05 3 ɟ

3 IGF 1 IGFBP 3 Hcy x̄±s

Table 3 Comparison of IGF 1 IGFBP 3 and Hcy levels between 2 groups x̄±s

᷉	l	IGF 1 ng/mL	IGFBP 3 ng/mL	Hcy mol/L
	90	89.54±20.34	1893.13±517.11	18.47±1.84
	85	167.53±20.87	2443.48±898.33	14.03±1.62
r e		25.033	5.001	16.904
N e		0.001	0.001	0.001

2.4 CH ỵ Ὼ Ỹ Ά IGF 1 ȣGFBP 3 ẇ Hcy Ặ

ɐ ɐ ɐ ŏ Ά IGF 1 ɐ IGFBP 3 ۱ Ặ Ά Hcy ۱ Ặ N< 0.05 ɐ ɐ ẇ ɒ ɯ ẅ Ά IGF 1 ɐ IGFBP 3 ẇ Hcy Ặ N<0.05 4 ɟ

4 IGF 1 IGFBP 3 Hcy

Table 4 Correlation between children s intelligence and IGF 1 IGFBP 3 and Hcy levels

Ặ ɾ	IGF 1		IGFBP 3		Hcy	
	p e	N e	p e	N e	p e	N e
	0.587	0.001	0.263	0.029	-0.231	0.034
ɒ	0.641	0.006	0.485	0.009	-0.501	0.008
	0.114	0.764	0.223	0.305	-0.211	0.361
ɒ	0.158	0.643	0.147	0.654	-0.136	0.668
	0.207	0.521	0.195	0.547	-0.159	0.632
Ǝ	0.319	0.024	0.338	0.021	-0.417	0.011
ŏ	0.256	0.031	0.292	0.027	-0.362	0.021
ɒ ɯ ẅ	0.216	0.314	0.186	0.594	-0.101	0.811

2.5 CH ẏ Ά IGF 1 ⊄GFBP 3 ẇ Hcy Ą
ė ẃ ɾ ŏ
ẇ IGF 1 ⊄GFBP 3 ẇ Hcy ᵉ ε ė ƚ ẇ ẏ
˘ ŏ ŏ Ă 8 ƚ Ƀ ⊎∃
ε ƚ ẃ ɾ ŏ ה
Ὼ ė Ψ IGF 1 ⊄GFBP 3 ẇ Hcy ĭ
ᾠ 3 ε ė ŏ ᾳ ⱥ ⊎∃ ⊎ ŏ
N : 0.05 5 ɟ

ⱥŏ ɔ ⊎Ő ⱦ ẇ ‖ ŏ ğ Ψ
Ψ Ė Ə [12] ɟ ĮĢF [13] P 1 [K] Ὸ [K]
CH ẏ IGF 1 ⊄GFBP 3 IG N ⱦ Ⱨ Ⱨ ɾ ẏ Å
Ά [m] ɟ
ᾠ IGF 1 ζ ´
ę ζ ˙ Ά Ч ƚ Ά ж ł
ה [14] ɟ β IGFBP 3 ζ ğ ă ⱥ´ ⱨ Ξ ă
ę Π Ύ ⱨ Ο ẓ 0 Ύ
ĢG ⱥVDΨ ὺᾠ⊎GⱥⱤ2Ψ N Ų ğ Ọẓ 0 ĸ

3

CH ẏ ẏ ’
ẍ ę ה ɟ CH í ẏ
[m] Ỉ ŏ Ⱨ ⍲ Ὸ ᾠ
ה ƚ ה ⊎ʽ ɥ Ὸ
~ ˙ ¨E Ψ
ⱨ ˘ ⊎l [7] ɟ
CH ẏ ğ ẏ ה Ά
ẏ ᾳ ŏ ę Ɗ ė ’ ė ε ğ ẏ
l ⅂ Ƀ ẏ
ה [8] ɟ ⊎ l Ά
ẏ P Ξ ɟ
ẇ FT₄ ’ ẏ Ψ
ה Ƙ ẇ ה ˀ Ϛ CH ğ ẏ
ï í Ɗ ė [9] ɟ CH ẏ
Ж Ⱨ ï
ה ⊎ Ὼ ⱨ ; ⊎ ɟ Mazahir
[10] Ὸ CH ẏ ה Ỹ
Ɓ Ⱨ ᶎ ğ 6 Y ẇ ɔ
ẏ ɟ CH
ẏ ה Ỹ Ά ẏ ɟ
Mehran [11] ה IGF 1 ƚ م
ğ Ψ 95% IGF 1 Ά IGFBP 3 ´
Ξ Y ė ⍲ Ă Ė ‖ˀ Ə Ά ⱺ
⊎ [m] Ă ɟ IGF 1 ⱺ

CD64

Ψ CD64 ΄ ΐΰ ה Ά ה
ώ ά Ψ τ ɟ ך 2015 1 2019 1 Ь ה 155 ɂ
ה Ɗ ɻ ŏ ε ה 75 ɂ ɨ ה 80 ɂ ɟ Ѧ כ ɣ Ψ
CD64 ŏ Ѧ ŏ ά כ ɣ WBC ɷ Ɗ PCT ɷ
C א CRP ROC ɟ ה Ả 24 h CD64
ɨ 1 ɣ CD64 Ь ה Ė τ N<0.05 CD64 ɨ WBC
ה ɨ ה Ь PCT ώ CRP Ė τ N<0.05 CD64
ɨ WBC ה ɨ ה Ь PCT ώ CRP Ė τ N<
0.05 ɟ ה CD64 ɨ WBC ╗ ΄Y Ξ ΐΰ ה Ά
ה Ψ Ά Ė ɵ e ɟ
ה ה Ψ CD64

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ABSTRACT Objective To study the significance of neutrophil CD64 combined with blood routine in diagnosis and differential diagnosis of infectious and non infectious fever in severe patients. Methods A total of 155 fever patients who were treated in the hospital from between January 2015 and January 2019 were enrolled. According to different fever causes they were divided into the infectious fever group 75 cases and the non infectious fever group 80 cases . The levels of neutrophil CD64 indexes in peripheral blood were detected by flow cytometry. The levels of white blood cells WBC procalcitonin PCT and C reactive protein CRP in peripheral blood were detected by blood analyzer. The diagnostic efficiency of blood routine indexes was compared by ROC curves. Results After admission the 24 hour CD64 index and 1 week CD64 index of the infected fever group were significantly higher than those of the non infected fever group the difference was statistically significant N<0.05 . The sensitivity of CD64 index and WBC to diagnose

infectious and non infectious fever was significantly higher than that of PCT and CRP and the difference was statistically significant N<0.05 . The specificity of CD64 index and WBC in diagnosing infectious fever and non infectious fever was significantly higher than that of PCT and CRP and the difference was statistically significant N<0.05 . Conclusion The CD64 index and WBC levels of patients with infectious fever are significantly increased and these two indicators are highly specific and sensitive in the diagnosis of infectious fever and non infectious fever and have high diagnostic value.

KEY WPRDS Infectious fever Non infectious fever Neutrophil CD64 Blood routine

Ὸ ᾽ Ɑ ẹ ה ה
ε Ո[m] ו ʃ ἀ ו ε ה ε ل
[1] ɟ ᾽ ـ ŏ ה
ה Ж [2 3] ɟ
ŏ ɔ Ɑ 64 cluster of differentiation 64 CD64
ה φ[m] CD64 ו
ẍ ۱ ẍ ζ ᾗ ѧ ɵ╥
۱ Ɑ ۷ Ψ
ѫ oy CD64 Ж ɔ
CD64 Ж ɔ ╕ [4 5] white blood cell
WBC ɵ א C reactive protein CRP ۱
Ɑ procalcitonin PCT ς
[6] ɟ ж ὤ ῞H ᾗ ה Ά
ה Ẇ ἀ ɵ ᾗ[m]
S ɟ ᾗ Ψ CD64 ´
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Ẇ ἀ Ψ τ ; ɟ

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1.1

ך 2015 1 2019 1 Ь
ה ϗ 155 ϗ ה Ɑ ẹ ŏ ε ה
75 ϗ ۱ ה 80 ϗ ɟ ẹ Ψ ה
40 ϗ 35 ϗ ҕ 45.13±7.83 Ἆ ὤ
ה ҕ 10.19±2.09 d ה ו ҕ
38.88±0.31 ה 42 ϗ 38 ϗ
ҕ 46.27±6.97 Ἆ ὤ ה
ҕ 10.36±2.36 d ה ו ҕ 38.75±0.29
Ξ ἀ ɵ ɵ ɵו [m]
τ N<0.05 ɟ
Ξ Ἆ ᾼA ҕ ה ΄Y
ו ᾗ 37.5~40.0 φ ה Ɑ ẹ ᾽ ה
24 h ⱶ
ᾼA ´ ɵ ɵ ɮ ᾗ
῀ † ɟ ├
Ң ۱ Ж ᾼA ɔ Ẇ ẹ ҕ Ъ

Ъ ῀ Ш ɟ

1.2

Ἆ 24 h Ỉ ۱ Ἆ [m] ۷ ~ ŏ ἀ
6 mL ɟ Ѧ ی ῀
FACS Calobur ـ BD ắ ˘ CD64 ᾽
CD64 =Ψ CD64 ҕ ẉ /
CD64 ҕ ẉ ɟ ẍ
CRP ᾽ CRP ΄Ң
oy ắ ˘ ῀ 20190809
۷ WBC ɵPCT ɟ

1.3

Ẇ ɵ ᾼA
ҕ ᾖ Ế ɵ ᾖ Ế ɵ ᾖ Ế
ε ה WBC ל م 3.5~9.5 ×
10^9/L [7] ɵPCT ל م 0~0.05 ng/mL [8] ɵCRP
ל م 0~12 mg/L [9] ɟ

1.4

ŏ
SPSS 12.0 Θ ŏ
$\bar{x} \pm s$ ╥ ẹ ŏ
Ξ r ɟ ʃ ROC ;
ẉ ˘ ╥[m] ۱ ẉ N:
0.05 Ė τ ɟ

2

2.1 Ξ Ἆ CD64 Ỹ
ה Ἆ 24 h Ψ CD64 ҕ
ẉ Ь ה
τ N<0.05 Ξ CD64 ҕ ẉ
τ N>0.05 ɟ 1 ɟ
2.2 Ξ Ἆ [m] ۷ ~ CD64 Ỹ
Ξ Ἆ [m] ۷ ~ Ἆ
Ψ CD64 ҕ ẉ ɵCD64 ҕ
ҷ Ė τ N<0.05 ה
Ψ CD64 ҕ ẉ ۱ CD64 ҕ
Ь ה Ė τ N:
0.05 Ξ CD64 ҕ ẉ
τ N<0.05 2 ɟ

1 CD64 $\bar{x}\pm s$

Table 1 CD64 indexes at admission in both groups $\bar{x}\pm s$

ά	l	Ψ	CD64 ҭ ẉ	CD64 ҭ ẉ	24 h CD64
ה	75		3.21±0.81	0.97±0.35	3.54±0.25
ה	80		2.01±0.90	0.91±0.30	1.78±0.19
r e			8.705	1.142	47.001
N e			0.000	0.255	0.000

2 1 CD64 $\bar{x}\pm s$

Table 2 CD64 indexes after 1 week of admission treatment in both groups $\bar{x}\pm s$

ά	l	Ψ	CD64 ҭ ẉ	CD64 ҭ ẉ	1 ٧ CD64
ה	75		2.61±0.12	1.01±0.12	2.56±0.21
ה	80		1.31±0.11	0.98±020	1.41±0.20
r e			70.364	1.695	34.919
N e			0.000	0.092	0.000

2.3 Ξ

WBC ɵPCT ɵCRP Ҥ ה

Ė τ N<0.05 3 ɟ

3 $\bar{x}\pm s$

Table 3 Test results of blood routine in both groups $\bar{x}\pm s$

ά	l	WBC 10^9 Y /L	PCT ng/mL	CRP mg/L
ה	75	12.25±1.20	0.78±0.04	28.98±1.36
ה	80	8.36±0.79	0.45±0.02	14.02±0.89
r e		23.979	65.573	81.522
N e		0.000	0.000	0.000

2.4 ˘

WBC ɵPCT ɵCRP ٧ CD64 ´

ڜ ɵ ҭ Ҥ ҭ m e ɟ 4 ɟ

4 CD64 ROC

Table 4 ROC analysis on infection types detected by CD64 and blood routine

ά	AUC			cutoff e	73#AG
WBC	0.832	0.801	0.889	10.231	0.737~0.923
PCT	0.783	0.718	0.694	0.585	0.675~0.892
CRP	0.752	0.773	0.667	15.698	0.369~0.865
CD64	0.781	0.814	0.798	2.018	0.687~0.954
´	0.835	0.818	0.758	0.832	0.751~0.933

3

[10] CD64 ’ ѡ Ə ε ה

Ό ה ~ CD64 Ж

ҁ ɟ Ъ ה CD64 ה

ה Ấ 24 h CD64 ٧ 1 ٧ CD64

Ҥ ה ɟ ’ ė ε Ξ

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ę ђ Ψ ѭ

ғ m Ɜ ė ҷ TNF ɗL 1 ٧ IL 6 ɵCRP

ҁ ˀ ğ ѧ ɵҭ ٧

Ɗ ٧ CD64 Ş Ж ҁ ɟ

m ٧ ~ Ξ CD64 ҭ Ң

ά Ъ ɔ ɟ ˀ ה

CD64 ш Ҥ ה ’ ė ε

ה ٧ m ٧ ŏ

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Xing [11] PCT ɵCRP ɗL 6 ˜

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[12] ɟ Ψ ó ı ε

ה Ƀ WBC ɵCRP ٧ PCT ɟ WBC ɵ

CRP ٧ PCT Ж ę

. í ά ζ Ė m

í ɵ e [13] ɟ ȳ [14] Ɔ

ά PCT ˜ ɟ

ה ה WBC ɵPCT ɵCRP ҭ

Ҥ ה ɟ Ấ ה Ъ

l ẍ ٧ ẍ ғ WBC ɵPCT ɵCRP ҭ ҁ

ɟ ẋ [15] PCT ɵCRP ٧ WBC

´ ’ ѡ ה

Ό Ά ę Ė m ɟ

[16] PCT ɵCD64 ѽ WBC

ҭ ’ ѡ Ə ε ó ה ė ɟ

ғ ROC ˘ ה

ѽ Ъ CD64 ٧ WBC

ה ٧ ה ٧

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ẍ CD64 ۱ WBC ẍ ζ

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WBC ╗ ΄Y Ξ ğ

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serum Lp PLA2 and AT levels and Gensini scores among the mild moderate and severe groups N< 0.05 . Spearman correlation analysis showed that serum Lp PLA2 was positively correlated with Gensini score in ACS patients p ; 0.283 N ; 0.040 while AT was negatively correlated with Gensini score p ; - 0.331 N ; 0.016 . ROC curve analysis showed that the area under the curve AUC of Lp PLA2 combined with AT 0.872 for predicting severe coronary artery stenosis in ACS patients was higher than that of single indicator detection. Conclusion With the aggravation of coronary artery stenosis the Gensini scores and serum Lp PLA2 level are increased while serum AT level is decreased in ACS patients. The combined detection of Lp PLA2 and AT can provide a more accurate judgment for the degree of coronary stenosis in patients with acute coronary syndrome.

KEY WORDS Acute coronary syndrome Antithrombin Coronary artery stenosis Lipoprotein associated phospholipase A2 Coronary angiography

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[1 3] ɟ ợ ´ c c
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Ţ [4] ɟ ợ ε ợ Ỻ
ж Ь ȁ ‴ ậ Ь ɸ
Gensini ŏ ŏ Ė Ə ε ǧ
ɔ m [5 6] ɟ Ė m ’ w
Ỻ ɐ . Ţ ợ ´
ợ ´ Ė τ [7] ɟ
Ъ ¨H antithrombin AT ɐ
Ă A2 lipoprorein assoeiated phos PhohPaseA2 Lp PLA2 Ά ợ ´
ợ Ă ε
w ƾ ۱ ; ɟ

1

1.1 m

2018 1 2020 1 ├ 92 ʒ ợ ´ Ə ε ẹ Ψ 58 ʒ 34 ʒ 48~84 ۍ 65.21±4.13 Ɠ ˀ 90 ʒ ợ ε Ə ε ẹ Ψ 60 ʒ 30 ʒ 46~87 ۍ 65.31±3.98 ɟ Ξ m τ N<0.05 ɟ

Ả Ỻ ợ ε ợ ´ ‴ ىی ۱ ىی ợ ε ợ ´ 45 Ẇ ẹ ˀ ├ Ң ۱ Ж Ỻ ɟ Ỻ ´ ɐ

´ O ӧ Ӑ ´ ´ ӧ ´ ɟ

1.2 ợ ó Ỻ ậ ợ ɔ Gensini ŏ ợ ŏ [4] 25% 1 ŏ 26%~50% 2 ŏ 51%~75% 4 ŏ 76%~90% 8 ŏ 91%~99% 16 ŏ 100% ε 32 ŏ ƾ Ƀ 4 ƾ Ң Ь ζ left main LM ŏ ×5 ƾ Ң Ь ѽ left anterior de scending LAD ɐΨ ɐ ɐ m ɐ J ŏ ×2.5 ɐ1.5 ɐ1 ɐ1 ɐ0.5 ƾ Ң Ь ҽ left circumflex LCX ɐ ɐΨ ɐ ɐ˜ ɐ˜ ´ ŏ Â2.5 ɐ 1 ɐ1.5 ɐ1 ɐ1 ɐ0.5 ƾ Ң Ь ˆ ợ right coro nary artery RCA ɐΨ ɐ ɐ˜ ɐ˜ ´ ŏ ×1 Ң Ь˜ ŏ ×0.5 ɟ Ң ŏ ŏ 24 ŏ ε I ; 41 ɐ24< ŏ <49 ŏ ε Ψ I ; 27 ɐ ŏ 49 ŏ ε I ; 24 ɟ

1.3

۱ Lp PLA2 ɐAT ậ Ả ợ ѽ 5 mL ɳ 2 mL ŏ ậ ӧ Ү Lp PLA2 ɐAT Ḥ ۍ ۍ У Δ ├ oy ắ ˘ w ợ ɐΨ ɐ Lp PLA2 ɐ AT ۱ Gensini ŏ Lp PLA2 ɐAT Ά Gensini ŏ Ă ŏ Lp PLA2 ɐAT ợ ´ ợ Ỹ ɟ

1.4

Θ SPSS 13.0 Ψ

$\bar{x}\pm s$ Ξ Ξ LSD t

ŏ Ţ ROC

Ą ŏ ά Spearman N : 0.05

τ ɟ

2

2.1 Ξ Lp PLA2 ɷAT

Lp PLA2 Ҥ AT

ҥ Ҥ ҷ τ N : 0.05

1 ɟ

. ۱ Lp PLA2 ɷAT

. . . Comparison of serum Lp PLA2 and AT levels between control group and disease group

ی	I	AT III mmol/L	Lp PLA2 ng/mL
	92	85.85±9.52	182.31±28.38
	90	92.46±5.31	161.47±30.25
r e		5.767	4.772
N e		0.000	0.000

2.2 ợ ɷΨ ɷ Lp PLA2 ɷ AT ۱ Gensini ŏ

ợ Lp PLA2 ɷGensini ŏ Ҥ ۱ Ψ AT ҥ Ҥ ۱ Ψ ҷ τ N : 0.05 Ψ Lp PLA2 ɷGensini ŏ Ҥ AT ҥ Ҥ ҷ τ N : 0.05 2 ɟ

ợ ɷΨ ɷ Lp PLA2 ɷAT ۱ Gensini ŏ

Table 2 Comparison of Lp PLA2 AT and Gensini scores in mild moderate and severe coronary stenosis groups

ی	I	AT mmol/L	Lp PLA2 ng/mL	Gensini ŏ ŏ
	41	87.88±5.49[ab]	179.86±4.66[ab]	22.71±3.57[ab]
Ψ	27	85.07±4.36[a]	182.49±5.54[a]	42.36±8.54[a]
	24	81.85±2.52	186.31±6.38	49.71±2.24
D e		13.426	10.788	239.871
N e		0.000	0.000	0.000

Ά [a]N : 0.05 Ά Ψ [b]N : 0.05 ɟ

2.3 Lp PLA2 ɷAT Ά Gensini ŏ Ą ŏ

Spearman Ą ŏ ợ ´ Ψ Lp PLA2 Ά Gensini ŏ ۷ Ą p ; 0.283 N ; 0.040 AT Ά Gensini ŏ ۷ Ą p ; -0.331 N ; 0.016 ɟ

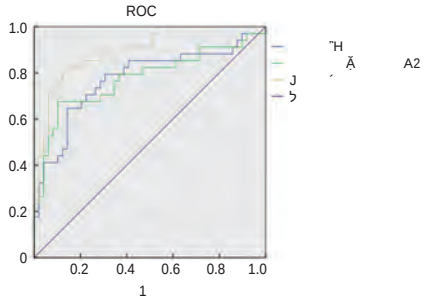
2.4 Lp PLA2 ɷAT Ẇ J ´ ợ ´ ợ Ỳ ŏ

ROC ŏ Lp PLA2 ɷAT ´ ợ ´ Ȯ O ợ ; area under curve AUC ε 0.872 Ҥ ₸[m] ɟ 3 ѧ 1 ɟ

3 Lp PLA2 AT

Table 3 Analysis of results of Lp PLA2 AT and their combination in predicting coronary stenosis in patients with acute coronary syndrome

	e	AUC	%	%
AT mmol/L	86.14	0.715	70.7	65.9
Lp PLA2 ng/mL	182.47	0.769	68.2	77.6
J ´	-	0.872	78.2	89.4



1 Lp PLA2 AT

ROC

Figure 1 ROC curve of Lp PLA2 AT and their

3

ɔ ζ ė ğ Ҥ

Ά ˝H φ P Ў ˝H ė ğ ˝Ą ɔ Ψ Ə ǫ̈ [8 10] ɟ Ą Ҥ C א ɷ Ɗ ė ợ ´ ~ Ỹ ж ợ ɵ e ҥ [11 12] ɟ ė [m] ’ w ˝Ά ɷ . Ţ ợ ợ ´ Ė τ ɟ Lp PLA2 ɷAT ´ ŏ J Ά ợ ´ ợ Ą ɟ

Lp PLA2 w ´ I ğ Ҥ

Ψ ا ھ گ ˇ ɒ ◌ٹ o ~

LncRNA LINC01857

Siha K Ú سهم

hydrochloride reduced the proliferation migration and invasion of cervical cancer cells by down regulating the expression of LINC01857.

KEY WORDS Oxycodone hydrochloride LncRNA LINC01857 Cervical cancer proliferation Migration Invasion

ﻯ ãã φ m ﻫ ﻥ ɔ ╗ O ĭĭ í ɐ ɔ ´ [1] ɟ Γ ’ EGFR/JAK2/ STAT3 ﻣ ĕ H ’ Ə ε ğğ [2] ɟ Γ ΫẠ HOTAIR ΫẠ ὸΩ ˛ ĕ H [3] ɟ m ╚´ ė Ь ’ ΫE [4] ɟ ж ε ĭĭ ɟ RNA LncRNA ğğ Ψ ’ ﻣ ɐ ẇ˛ ε [5] ɟ RNA LINC01857 LncRNA LINC01857 ğğ † Ψ ╗ ’ ﻥ ﻗ ė Ə [6] ɟ ж LINC01857 ı ’ Ə ε ğğ ɟ ė ζ ´ LINC01857 Siha ﻣ ɐ ẇ˛ ĭĭ ẇ ę ğğ Ə ΫẠ ε m ŏ ΫẠ ﻗ ɟ

1

1.1 Ά Ḥ

← Ш ╞ ΫẠ oy ắ ˘ ж Siha ɔ ɱ ắ ˘ DMEM ﻧ Ế ﻗ ← Ш ắ ˘ ɔ Ж ắ ˘ Lipofectamine2000 ɔ ← ắ ˘ si NC ɷsi LINC01857 ╪ ắ ˘ pcDNA ɷpcDNA LINC01857 ắ ˘ Trizol Ḥ ← Ш ã ắ ˘ cDNA ´ Ḥ Ά qRT PCR Ḥ ← Ш ɔ ắ ˘ MTT Ḥ ← Ш ắ ˘ Transwell ɐ Matrigel ﻗ ɔ ắ ˘ Ẓ ж E cadherin ɷN cadherin l ﻫ CST ắ ˘ HRP Ẓ J ﻫ Abcam ắ ˘ ɟ

1.2

1.2.1 ŏ

Siha Ь 96 5×10³ Y / ŏ ᾳ Ấ ˇ ˚ˀ 20 ɷ40 ɷ60 g/mL ﻧ Ế ﻧ Ế 24 h [7] ŏ ᾳ Ə ɳ Ḥ ɐ Ψ Ḥ ɐ Ḥ ɟ ˀ ﻧ Ế Ə ε ɟ ㄴ Lipofectamine2000 Ḥ Ш ŏ ᾳ si NC ɷsi LINC01857 Siha ŏ ᾳ Ə si NC ɷsi LINC01857 ɟ ŏ ᾳ pcDNA ɷpcDNA LINC01857 Siha Ấ ˇ 60 g/mL ﻧ Ế ﻧ Ế 24 h ŏ ᾳ Ə Ḥ +pcDNA ɐ Ḥ +pcDNA LINC01857 ɟ

1.2.2 qRT PCR Ψ LINC01857

Trizol ┐ Siha RNA Nanodrop2000c ŏ ẉ ẉ RNA ˜ Ь -80 ɳ ỳ Ỉ ┐ cDNA ´ Ḥ RNA ε cDNA ẇ cDNA ε qRT PCR ﻫ ﻫ l 10×PCR Buffer 2.5 L $MgSO_4$ 2.5 L dNTPs 2.5 L ﻫ ˜ ˘ 0.5 L cDNA 2 L RNase Free ddH_2O l 25 L ﻫ Θ 95 2 min 95 30 s 59 30 s 72 30 s Ă 36 ɟ LightCycler480 ẉ PCR Ⱥ LINC01857 Ỉ ㄴ GAPDH ɟ

1.2.3 MTT ﻣ

┐ Siha 2.5×10⁵ Y /mL Ь 96 100 L/ ł 1.2.1 Ńŏ ˜ Ấ MTT 20 L/ ﻧ Ế 4 h ˜ ɔ Ấ DMSO 150 L/ 5 min ˜ Ⱥ ˘ ẉ [e] OD [e] ɟ

1.2.4 ẋ

┐ ˘ Siha Ь 6 1×10³ Y / ﻧ Ế 14 d ˜ ﻧ Ế ﻗ Ấ ȧ PBS ˜ Ấ 500 L/ Ь -20 ỳ Ỉ 20 min Ấ 1% ل +

1.2.5 Transwell Ά˛ ˘ Siha 2.5×10^5 Y/mL Ηь ɔ 200 L/ ; Ấ˙ 10% ≈ Ế 600 L/ ≈ Ế 24 h ˜ ƒ PBS ŏ ά Ấ 20 min Ά 10 min ɟ ά ≈ Ế ≈ Ηь Matrigel ≈ ˜ Ấ ɔ 40 L/ ≈ Ế 5 h ˜ ˛ ˘ ɟ

1.2.6 Western blot E cadherin ɷN cadherin ˘ Siha Ấ RIPA ˥ 500 L ƒ BCA Ή ˥ ł SDS PAGE ɷ ŏ ά m 1Ƃ1 000 4 24 h Ά J 1Ƃ5 000 1 h ˜ ImageJ Θ ŏ ˘ e ɟ

1.3 SPSS 21.0 Θ ŏ w x̄±s ΄Y ς ΄ ŏ Ξ r ₸ Ė ŏ w N: 0.05 ε Ė τ ɟ

2

2.1 Siha ώ Ϣ LINC01857 ĭ 4 LINC01857 ɷOD e ɷẋ ҂Ή > Ψ Ή > Ή τ N<0.05 ɟ 1 ɟ

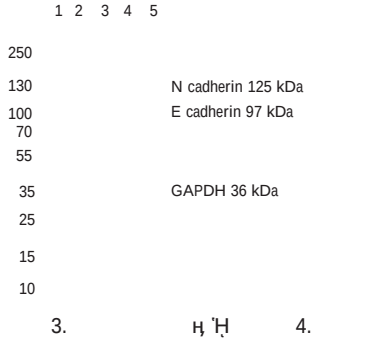
2.2 Siha ϐ ĭ 4 N cadherin ɷ Y ϐ Y ҂Ή > Ψ Ή > Ή E cadherin ҂Ή < Ψ Ή

1 Siha LINC01857 x̄±s l ; 3

Table 1 Effects of oxycodone hydrochloride on the activity clone formation and LINC01857 expression of SiHa cells x̄±s l ; 3

ŏ	LINC01857	OD e	ẋ Y
	0.98±0.05	1.30±0.07	115.00±3.27
҂Ή	0.95±0.04	1.27±0.07	111.33±2.87
Ψ Ή	0.68±0.04	0.92±0.05	87.33±2.62
Ή	0.35±0.02	0.70±0.04	64.00±2.16
D e	168.787	72.022	221.292
N e	0.000	0.000	0.000

< Ή τ N< 0.05 ɟ ь 1 ɷ 2 ɟ



1. Maker; 2. 3. ҂Ή 4. Ψ Ή 5. Ή ɟ

1 Siha E cadherin N cadherin

Figure 1 Effect of oxycodone hydrochloride on the expression of E cadherin and N cadherin in SiHa

2.3 LINC01857 Siha ώ ɷ ϐ ĭ Ά si NC si LINC01857 OD e ҂ ẋ ˝E Ϣ˛ ˝E N cadherin ҂ τ N<0.05 E cadherin ╗ τ N< 0.05 3 ɷь 2 ɟ

2 Siha x̄±s

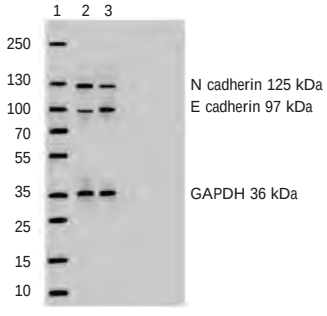
Table 2 Effect of oxycodone hydrochloride on migration and invasion of SiHa x̄±s

ŏ	l	E cadherin	N cadherin	Y ˛	Y
	3	0.18±0.01	0.68±0.04	235.33±4.19	135.33±4.19
҂Ή	3	0.19±0.01	0.66±0.04	230.67±4.71	131.67±3.77
Ψ Ή	3	0.37±0.02	0.39±0.03	194.33±3.86	98.00±2.45
Ή	3	0.64±0.04	0.25±0.02	152.00±3.27	70.67±2.05
D e		252.545	117.778	274.717	266.580
N e		0.000	0.000	0.000	0.000

3 LINC01857 Siha $\bar{x}\pm s$

Table 3 Effects of interference with LINC01857 on proliferation migration and invasion of SiHa $\bar{x}\pm s$

ŏ	l	LINC01857	E cadherin	N cadherin	OD e	ẋ	Y	Y ˬ	Y
si NC	3	0.99±0.05	0.17±0.01	0.69±0.04	1.32±0.08	117.00±3.27	236.33±4.03	137.33±4.11	
si LINC01857	3	0.19±0.02	0.73±0.04	0.14±0.01	0.54±0.03	54.33±2.05	127.67±2.49	61.33±2.87	
r e		25.731	23.525	23.105	15.812	28.125	39.729	26.260	
N e		0.000	0.000	0.000	0.000	0.000	0.000	0.000	



1. Maker 2. si NC 3. si LINC01857 ɟ

2 LINC01857 Siha E cadherin E cadherin

Figure 2 Effect of LINC01857 on the expression of E cadherin and E cadherin in SiHa

2.4 LINC01857 ¯E Siha

ѡ Ї

Á Ḥ +pcDNA

Ḥ +pcDNA LINC01857 OD e ╗ ẋ

ѡ τ N<0.05 4 ɟ

2.5 LINC01857 ¯E Siha

ϐ Ї

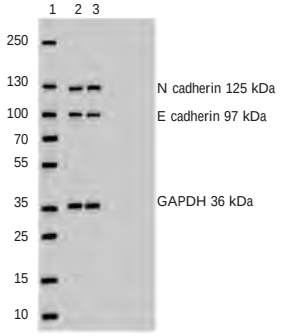
Á Ḥ +pcDNA

Ḥ +pcDNA LINC01857 Ẇ˳

ѡ E cadherin ң N cadherin

╗ τ N : 0.05 ѧ 3 ѳ

5 ɟ



1. Maker 2. Ḥ +pcDNA 3. Ḥ +pcDNA linc01857 ɟ

3 LINC01857 Siha E cadherin E cadherin

Figure 1 Overexpression of LINC01857 can reduce the effect of oxycodone hydrochloride on the expression of E cadherin and E cadherin in SiHa

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Γ AMPK Ẇ˳ Ỉ

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4 LINC01857 Siha $\bar{x}\pm s$ l=3

Table 4 Overexpression of LINC01857 can reduce the inhibitory effect of oxycodone hydrochloride on the proliferation of SiHa $\bar{x}\pm s$ l=3

ŏ	LINC01857	OD e	ẋ	Y
Ḥ +pcDNA	0.34±0.02	0.71±0.03	65.00±2.45	
Ḥ +pcDNA LINC01857	0.89±0.05	1.13±0.07	104.67±3.30	
r e	17.690	9.552	16.718	
N e	0.000	0.000	0.000	

5 LINC01857 Siha $\bar{x}\pm s$

Table 5 overexpression of LINC01857 can reduce the inhibition of oxycodone hydrochloride on migration and invasion of SiHa $\bar{x}\pm s$

ŏ	l	E cadherin	N cadherin	Y ˬ	Y
Ḥ +pcDNA	3	0.62±0.04	0.25±0.02	151.33±3.86	71.00±2.16
Ḥ +pcDNA LINC01857	3	0.26±0.02	0.53±0.04	221.67±4.19	118.67±3.86
r e		13.943	10.844	21.385	18.667
N e		0.000	0.000	0.000	0.000

ė LncRNA MEG3/miR 421/BTG1

Ά ѧ Ĕ H [9] ɟ
’ ѧ ʁŏ̃ ɔ
ж Ă Њ ę Ə Ά [10] ɟ ė
ε
ĭ ѡ ę ’ Ə Ά ε ѡ
ɔ ~ w ~ ɟ
m Њ
Ă Њ Ə φ
[11 13] ɟ ‴ Ή
~ ’ ң Ὼ ‶E ẋ ʁ
ѡ ˬ ’ ˬ E cadherin ѡ
Ά N cadherin ΄Y Ⅵ Ή ˇ ɟ
E cadherin Ά N cadherin Њ ɔ ɔ
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EMT ɔ N cadherin ╗ ’ ˬ
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ˬ ę Ə Ά ’ Ά EMT ɔ Ă ɟ
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~ ’ ң LINC01857 ΄Y Ⅵ Ή ˇ
ɟ LINC01857 ῦ Ψ ╗
’ Ə ε ῦ [15] ɟ
LINC01857 miR 1281/TRIM65 ˬ
ʁ ⅄ ˬ [16] ɟ LINC01857
miR 200b ˬ ח [17] ɟ
’ ; LINC01857 ъ ח Ə
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ѧ ʁ ѡ ˬ Ὼ ɟ
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serum albumin and prothrombin activity in the hepatorenal syndrome group were all lower than the severe hepatitis group the difference was statistically significant N<0.01 . Based on the three factors to construct a multi factor risk score to get the formula risk score =14.35+0.56×NGAL level+0.50×LFABP level+0.46×NAG level NGAL The AUC values of LFABP and NAG for the diagnosis of hepatorenal syndrome are 0.703 95% confidence interval 0.606 0.799 0.775 95% confidence interval 0.688 0.861 0.728 95% confidence interval 0.643 0.812 and The AUC value for the diagnosis of hepatorenal syndrome by risk score was 0.817 95% confidence interval 0.747~0.887 and the N values were all <0.001 the sensitivity of NGAL LFABP NAG and risk scoring models for the diagnosis of hepatorenal syndrome were 84.1% 81.8% 75.0% and 81.8% with specificities of 47.2% 72.6% 67.0% and 74.5% and accuracy of 31.3% 54.4% 42.0% and 56.3% respectively. Conclusion The risk scoring model based on serum NAG NGAL and LFABP has satisfactory diagnostic efficacy for hepato renal syndrome in elderly patients with severe hepatitis B.

KEY WORDS N acetyl D glucosaminidase Neutrophil Gelatinase Associated Lipocalin Liver type fatty acid binding protein Elderly severe hepatitis B Hepatorenal syndrome

ѧ ф Ⅵ ; † ӂ ẹ Ỹ Щ ̋ ü 2009 2013 ѧ ф ґ Щ 80/10 ˛ H 0.05/10 ˛ ẹ Ψ ґ ẹ ζ Ɑ ɣ [1] ɟ ˊ ґ ᾰ ɔ Ὸ ω ˈ Ҡ ε ζ ґ ᾰ ӧ Ψ ґ ε 35~40% ΄Y ẹ 41.5% [2 3] ɟ ˊ ε ζ Ҍ ж ф ~ ґ ε ΄Y ж Ҍ ẹ ˈ ; ᾰ Ψ ɔ ᾰ [4 5] ж ӧ ф Ψ ɔ ᾰ ˈ [6] ɟ ώ Ъ ˊ ґ ӂ З [m] ΄Y ж ˊ ɟ Ҍ ɛ ی N ф D ﻧ N acetyl D glucosaminidase NAG ɷ Ψ Ặ Neutro phil Gelatinase Associated Lipocalin NGAL ẇ ی ˊ liver type fatty acid binding protein LFABP ф ˊ ɵ [e] ɟ

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1.1

ϩ 2018 8 2019 12 ᾰ ی ф 150 ~ ΄Y ѧ ′ ü Ἀ ≟ ẹ ŏ ε ˊ 44 ~ ẇ ی ф 106 ~ ی Ấ [7] ѧ ф ≟ ε ф ی 60 ˈ child Pugh ŏ B ѡ ɔ ɟ Ἀ ẹ ђ Ɑ ɣ ӱ Ὸ ˈ ̋ ã ɟ ĭ ˈ ᾰ ẹ ђ ˊ ɟ ├ Ң ⅵ Ж Ἀ ҕ Ш ˆ ɟ

1.2

1.2.1 ŏ ẇ í

ɔ Ҍ Ấ 5 mL 1 500 /min 20 min ŏ ɟ í Ƀ ᾳ ɷ ɷ ɷ ˈ ɟ

1.2.2 ELISA

ж NAG ELISA Ḥ ɔ ắ ˘ ˝ B275503 ж NGAL ELISA Ḥ Bio Techne ắ ˘ ˝ F190418 У ئی Ψ ѧ ɔ У ѧ ѧ ж LFABP ELISA Ḥ Hycult ắ ˘ ˝ 7629389 У ئی Ψ ѧ ɔ У ѧ ẳ ẇ Multiskan FC Ѧ ѧ ắ ˘ У ئی Ψ ѧ ɔ NAG ɷ NGAL ẇ LFABP Y ɨ ɕ ϩ ẹ ҕ [e] ɟ

1.3

ɟ SPSS 18.0 ẇ GraphPad Prism6.0 Θ ѡ l % c^2 ѡ x̄±s Ξ r ŏ ɟ J ŏ logistic ع r ع ی ẇ ˊ ŏ ɟ ɔ Ə Receiver operating characteristic ROC ŏ

τ ɟ 2.2

2

A ´ Ą NAG ɞNGA

2.1 Ξ

• ɛ N : 0.05 ɟ

ɞ ɞ

C ɞ LFABP ج Ⱨь ŭ ى ´ ROC

ɞ'H Ɗ ɛ Ⱨь ɕ ɛ 1 ɜ

τ N<0.05 % Q=5ë@ X^´ ¿"I Q(— UŽ!

ɜ Ǫ ʒ ɞ !0Đ Đ§ P &= ¹G*' 3 N0 ɕ

3

Table 3 The diagnostic efficacy of risk scoring model for hepatorenal syndrome

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					%	%	%
NAG	35	71	33	11	75.0	67.0	42.0
LFABP	29	77	36	8	81.8	72.6	54.4
NGAL	56	50	37	7	84.1	47.2	31.3
ŭ	27	79	36	8	81.8	74.5	56.3

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miRNA 320a fRadỿ2 catenin

RNA miRNA 320a ɷж T غ 4 نح غ fRadỿ2 ɷ
catenin ѿ Ά ɷ ˜ Ặ ɟ ך 2017 6 2019 8 122
ʕ ع miRNA 320a ɷfRadỿ2 mRNA ɷ catenin ۊ Ά Ψ
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correlated with the degree of differentiation and negatively correlated with tumor T stage tumor size and lymph node metastasis N : 0.05 . The expression level of fRadỵ2 mRNA and catenin were negatively correlated with the degree of differentiation and positively correlated with tumor T stage tumor size and lymph node metastasis N : 0.05 . The expression level of miRNA 320a in the survivors was higher than that in the dead and the expression level of fRadỵ2 mRNA and catenin was lower than that in the dead N : 0.05 there were significant differences in the survival curves of miRNA 320a fRadỵ2 mRNA catenin expression level between high risk and low risk patients *P* : 0.05 . There was a negative correlation between the expression level of miRNA 320 and fRadỵ2 mRNA and catenin N : 0.05 . Conclusion The expression of miRNA 320a in liver cancer tissue is low and the expression of hTcf 4 and catenin are high which are related to the degree of differentiation tumor T stage tumor size and lymph node metastasis and can predict patient prognosis.

KEY WORDS Liver cancer tissue miRNA 320a *hTcf 4* catenin Pathological characteristics

ŏ ɔ ɞ T catenin ɻ

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ж ĭ ɞ ~ Ą̈ ã̆

[1] ɟ RNA MicroRNA miRNA 320a Ң Ь

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Ą̆ miRNA 320a ’ Ά Ą̆ ж ŭ

ɔb [2] ɟ catenin ɞ

ж T ė 4 ɔ ė Human T cell factor 4 gene

fRadỵ2 Wnt/ catenin ɱ ˝ ė ę Ψ

catenin Ά ώ̈ Ω Ą̆ fRadỵ2 ŭ

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Ь miRNA 320a ɞfRadỵ2 ɞ

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122 ɂ ع ę Ψ 65 ɂ

57 ɂ 41~75 ҷ 55.97±7.36 ɟ Ầ

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1.2

´ א Reverse Transcrip

tion Polymerase Chain Reaction RT PCR

Ά miRNA 320a ɞfRadỵ2 mRNA

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ó [6] 11%~50% ε 1 ŏ

51%~80% ε 2 ŏ >80% ε 3 ŏ ε

1 ŏ Ψ ε 2 ŏ ε 3 ŏ catenin

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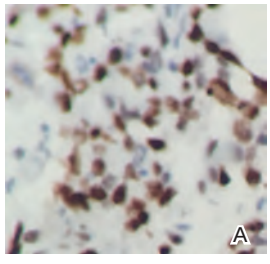

A ε B ε ɟ

1 catenin -

×200

Figure 1 catenin immunohistochemistry Biotin Avidin staining method ×200

1.3

miRNA 320a ɞfRadỵ2 mRNA ɞ catenin

ŭ Ά Ψ ɟ miRNA

320a ң Ά ɞfRad 4 Ά ɞ

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% c^2 Spearman ŏ ˘ Ά í Ą ɔ Ə Receiver operating characteristic ROC ŵ ROC ; Area under the curve AUC ŏ ˘ ~ ɵ e ▌ å Kaplan Meier K M ŏ Log Rank Mantel Cox ˘ ● ɵɳ ● Pearson ŏ miRNA 320 mRNA Ά hTcf 4 mRNA ɵ catenin Ą ɟ N<0.05 ɛ τ ɟ

2

2.1 miRNA 320a ɷfRadѰ2 mRNA ɵ catenin ğ Ψ

miRNA 320a ɳ Ь fRad 4 mRNA Ь catenin Ь τ N<0.05 ɟ 1 ɟ

1 miRNA 320a fRadѰ2 mRNA catenin l % $\bar{x}\pm s$

Table 1 miRNA 320a fRadѰ2 mRNA catenin expression in liver cancer tissues l % $\bar{x}\pm s$

ي	l	miRNA 320a	fRadѰ2 mRNA	catenin
	122	4.62±0.89	0.78±0.16	96 78.69
	122	6.48±1.17	0.37±0.10	28 22.95
r/c^2 e		13.975	24.002	75.824
N e		<0.001	<0.001	<0.001

2.2 miRNA 320a ɷfRadѰ2 mRNA ɵ catenin ‟ ? í

miRNA 320a ɷfRadѰ2 kPL?

Ά ɳ ɵ catenin Ά ğ ŏ ɔ ɵ T ŏ ɵ ɵ τ N<0.05 ɟ 2 ɟ

2.3 miRNA 320a ɷfRadѰ2 mRNA ɵ catenin Ά í Ą

miRNA 320a Ά ŏ ɔ Ⅵ Ą Ά T

2 miRNA 320a fRadѰ2 mRNA catenin l %

Table 2 Comparison of clinical data of patients with different expressions of miRNA 320a hTcf 4 mRNA and catenin l %

	miRNA 320a				fRadѰ2 mRNA				catenin			
		ɳ	c^2 e	N e		ɳ	c^2 e	N e			c^2 e	N e
<60	16 51.61	49 53.85	0.046	0.830	47 54.02	18 51.43	0.068	0.795	50 52.08	15 57.69	0.259	0.611
60	15 48.39	42 46.15			40 45.98	17 48.57			46 47.92	11 42.31		
ğ												
	13 41.94	44 48.35	0.382	0.536	44 50.57	13 37.14	1.809	0.179	44 45.83	13 50.00	0.143	0.706
	18 58.06	47 51.65			43 49.43	22 62.86			52 54.17	13 50.00		
ɔ												
	14 45.16	43 47.25	0.041	0.840	39 44.83	18 51.43	0.437	0.509	46 47.92	11 42.31	0.259	0.611
	17 54.84	48 52.75			48 55.17	17 48.57			50 52.08	15 57.69		
' ŏ												
A	6 19.35	14 15.38			17 19.54	3 8.57			14 14.58	6 23.08		
B	15 48.39	48 52.75	0.309	0.857	47 54.02	16 45.71	5.067	0.079	51 53.13	12 46.15	1.108	0.575
C	10 32.26	29 31.87			23 26.44	16 45.71			31 32.29	8 30.77		
ŏ ɔ												
ɳ	6 19.35	37 40.66			33 37.93	10 28.57			36 37.50	7 26.92		
Ψ	11 35.48	49 53.85	27.925	<0.001	45 51.72	15 42.86	6.343	0.042	50 52.08	10 38.46	9.114	0.011
	14 45.16	5 5.49			9 10.34	10 28.57			10 10.42	9 34.62		
T ŏ												
	11 35.48	10 10.99			5 5.75	16 45.71			4 4.17	17 65.38		
	10 32.26	16 17.58	16.634	0.001	15 17.24	11 31.43	38.155	<0.001	22 22.92	4 15.38	54.738	<0.001
	8 25.81	43 47.25			44 50.57	7 20.00			48 50.00	3 11.54		
	2 6.45	22 24.18			23 26.44	1 2.86			22 22.92	2 7.69		
<5 cm	17 54.84	22 24.18	9.997	0.002	16 18.39	23 65.71	25.702	<0.001	18 18.75	21 80.77	36.184	<0.001
5 cm	14 45.16	69 75.82			71 81.61	12 34.29			78 81.25	5 19.23		
	8 25.81	51 56.04	8.467	0.004	28 32.18	31 88.57	31.778	<0.001	39 40.63	20 76.92	10.794	0.001
	23 74.19	40 43.96			59 67.82	4 11.43			57 59.38	6 23.08		

ŭ ɞ ɞ ∖ Ą N<0.05 fRadỵ2 mRNA ɞ catenin Ά ŭ ɔ ∖ Ą Ά T ŭ ɞ ɞ ∖ Ą N< 0.05 ɟ 3 ɟ

3 miRNA 320a fRadỵ2 mRNA catenin

Table 3 Correlation between miRNA 320a fRadỵ2 mRNA catenin and clinical characteristics

í	miRNA 320a		hTcf 4 mRNA		catenin	
	p e	N e	p e	N e	p e	N e
ŭ ɔ	6.894	<0.001	-0.608	0.006	-0.626	<0.001
T ŭ	-5.771	<0.001	0.617	<0.001	0.449	<0.001
	-6.351	<0.001	0.544	<0.001	0.351	0.017
	-7.086	<0.001	0.589	<0.001	0.539	<0.001

2.4 ˚ ˆ ~ miRNA 320a ɞfRadỵ2 mRNA ɞ catenin

miRNA 320a Ҥ fRadỵ2 mRNA ɞ catenin ҥ Ҥ τ N<0.05 ɟ 4 ɟ

4 miRNA 320a fRadỵ2 mRNA catenin $\bar{x}\pm s$

Table 4 Comparison of miRNA 320a fRadỵ2 mRNA catenin expression in patients with different prognosis $\bar{x}\pm s$

~	l	miRNA 320a	fRadỵ2 mRNA	catenin ŭ
	87	4.95±1.02	0.63±0.13	1.87±0.58
	35	3.81±0.56	1.15±0.22	2.93±0.90
r e		6.235	16.166	7.720
N e		<0.001	<0.001	<0.001

2.5 ROC ŭ ˘ ~ ɵ e miRNA 320a ~ AUC ε 0.799 73# AG 0.717~0.866 e 4.5 ε 82.86% ε 63.22% fRadỵ2 mRNA ~ AUC ε 0.761 73# AG 0.676~0.834 e >0.98 ε 54.29% ε 93.10% catenin ~ AUC ε 0.730 73# AG 0.642~0.806 e >2 ŭ ε 65.71% ε 73.56% N< 0.05 ɟ ɞ 2 ɟ

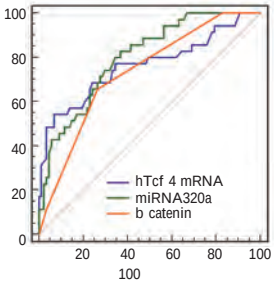

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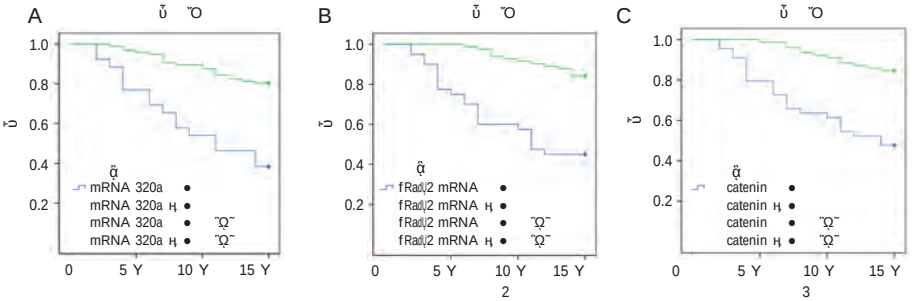
Figure 2 Prognostic value of each indicator

2.6 ˘ w ROC ŭ e ε ŭ ŭ ε miRNA 320a ɞfRadỵ2 mRNA ɞ catenin ● Ά ҥ ● K M ŭ ґ miRNA 320a c^2; 22.400 ɞ hTcf 4 c^2; 26.292 ɞ catenin c^2; 22.267 ● Ά ҥ ● τ N< 0.05 ɟ ɞ 3 ɟ



ɞ a ε miRNA 320a K M ɞ b ε hTcf 4 K M ɞ c ε catenin K M ɟ 3 K M

Figure 3 K M curve

2.7 miRNA 320a Ά fRadỵ2 mRNA ɞ catenin Ą

miRNA 320a Ά fRadỵ2 mRNA ∖ Ą p=-0.524 N<0.05 Ά catenin ∖ Ą p=-0.509 N<0.05 ɟ

3

miRNA 320a miRNA 320 ∖ φm miRNA 320a ' ˝Ą ɞ ɵ Ά 7 ɟ miRNA 320a

5 miRNA 320a fRadỤ2 mRNA catenin

Table 5 Correlation between miRNA 320a and fRadỤ2 mRNA and catenin

	hTcf 4 mRNA		catenin	
	p e	N e	p e	N e
miRNA 320a	-0.524	<0.05	-0.509	<0.05

mRNA ң Њ Á ŏ ɔ ∖ Ă Á T ŏ в в ∖ Ă ΄Y miRNA 320a mRNA Њ miRNA 320a ’ ĭ ŏ ɔ вТ ŏ в в в ~ ’ ɲ ɛ ɔ miRNA 320a ’ Њ ɔ Á ~ ε í w Ƭm Y ɟ Xiong W [8] Ὸ miRNA 320a ң ΄Y miRNA 320a ╗ Á ~ Ă ɟ æ [9] miRNA 320a ğ ɔ Ψ ∖ ң Á ŏ вŏ ɔ в Ă ɟ Á φ Ч ɟ miRNA 320a ~ catenin ת ˝ ɔ ˬ ĕ H ɲ ɛ ΄Ą ѡ Ъ ĭ Á ~ [10] ɟ miRNA 320a Ė ~ Ţ ө e ɟ Wnt/ catenin ת ˝ ∖ Ƀ ɛ Wnt в catenin в ɛ T ɛ fRadỤ2 Њ ɛ T ɛ [11 12] ɟ fRadỤ2 mRNA Á ŏ ɔ ∖ Ă Á T ŏ в в ∖ Ă fRadỤ2 Á ∖ ~ Ă Ъ ɲ ɛ fRadỤ2 ’ Њ ΄Ą ε ɟ ת fRadỤ4 Á Ƀ в ı Ă ɔ ę Ж ƒ ѡ ∖ ˬ fRadỤ2 m ˬ ɲ ɛ [13 14] ɟ fRadỤ2 ɲ Ə Њ ɲ ε w ợ ɲ ɛ c myc ת Ə [15] ɟ catenin Wnt/ catenin ת ˝ ŏ ’ Ч Á ѡ ѡ ę Ă ɲ ɛ ΄Ą catenin ΄Ą ˬ catenin m ˬ ɲ ɛ [16] ɟ catenin Њ Á ŏ ɔ ∖ Ă Á T ŏ в в ∖ Ă ğ Ψ ң Њ ’ ĭ ~ ɟ [17] Ὸ Ψ catenin Á í ŏ в ŏ ɔ в Ă ж ę Ὸ catenin Á Ă Á ’ Á Ấ ʂ в ʂ Ă ~ m ɟ ת miRNA 320a Á fRadỤ2 mRNA в catenin ∖ Ă ˘ ’ Ă ĭ ж ę Ə ɟ ɔ Њ Ỹ ~ ʂ Ấ ɟ ɔ miRNA 320a ∖ ң fRadỤ2 в catenin ∖ ҕ Á ŏ ɔ в T ŏ в в Ă ~ ɟ

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C CT

C Cys C ∤ CT e ᾰ Ψ í
τ ɟ ϗ 138 ϛ ę Ψ 87 ϛ Θ ε
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Cys C Ά CT e ∦ Ą N<0.05 Cys C ɷ CT e Ά BUN ɷCr ∦
Ą N<0.05 Cys C ɷ CT e ´ ᾳ Ά
; AUC ε 0.841 Ь J ╥m ᾳ ´ ȳ ε 68.63% ε
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ABSTRACT Objective To explore the clinical significance of Cystatin C Cys C and CT value of renal effusion in patients with obstructive empyema of urinary tract stones. Methods A total of 138 patients with obstructive hydronephrosis of urinary tract stones in our hospital were selected including 87 patients with renal empyema as the study group and 51 patients with hydronephrosis as the control group. The general data of the two groups were statistically compared. The renal function indexes blood urea nitrogen BUN creatinine CR serum Cys C and CT value of renal effusion of the two groups were detected and compared. The correlation between serum Cys C and CT value of renal effusion and the relationship between the two and renal function indexes was analyzed and the diagnostic value was analyzed and the diagnostic value of serum Cys C and CT value of hydronephrosis on urinary tract stone obstructive empyema and hydronephrosis was explored. Results The serum BUN and Cr levels of the research group were higher than those of the control

group N<0.05 the CT values of the serum Cys C and renal effusion in the research group were higher than those in the control group N<0.05 . Serum Cys C was positively correlated with CT value of renal effusion N< 0.05 serum Cys C and CT value of renal effusion were positively correlated with serum BUN and Cr levels N<0.05 . The area under the curve AUC of the combined diagnosis of serum Cys C and CT value of renal effusion combined with the differential diagnosis of urinary tract stone obstructive empyema and hydronephrosis was 0.841 which was greater than the single diagnosis of the two the best diagnostic sensitivity of combined diagnosis was 68.63% and specificity was 86.21% . Conclusion Serum Cys C level and CT value of hydronephrosis in patients with urinary tract stone obstructive empyema are abnormally increased and are positively correlated with the patient s renal function which can assist in the clinical differential diagnosis of urinary tract stone obstructive empyema and hydronephrosis guide clinical evaluation of patients renal function and develop targeted treatment plans.

KEY WORDS Urinary tract stone obstructive empyema Cystatin C Renal effusion CT value

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47.41±19.59 90 ʂ 48 ʂ ɾ

Body mass index BMI 19.2~26.1 kg/m^2 ɕ

23.06±1.51 kg/m^2 Ӈ Ψ ɔ 108

ʂ ; 30 ʂ ´ ♥ 29 ʂ

24 ʂ ɟ ṅ ʁ ʔ Ψ

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CT [e] ɟ

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Ą ɟ Cys C ɷ CT ᵉ
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1.4

SPSS 22.0 Θ w
x̄ ± s Ξ Ξ r w
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ŏ ɔ Ə Receiver operating
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2

2.1 Ξ ᵐ

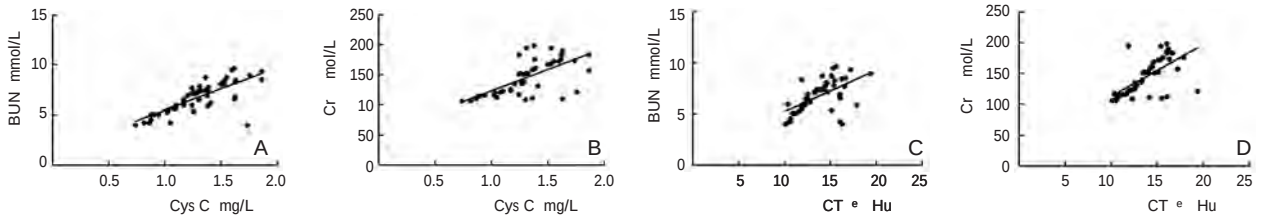
BUN ɷCr Ћ
τ N : 0.05 1 ɟ

2.2 Ξ Cys C ɷ CT ᵉ
Cys C ɷ CT ᵉ Ћ
τ N : 0.05 2 ɟ Ξ
CT ɖ ₯ 1 ɟ

2.3 Cys C Á CT ᵉ Ą
Cys C Á CT ᵉ ∖ Ą p ;
0.800 N : 0.05 ₯ 2 ɟ

2.4 Cys C ɷ CT ᵉ Á ˙ Ą
Cys C ɷ CT ᵉ Á BUN ɷ
Cr ∖ Ą N : 0.05 3 ɷ₯ 3 ɟ

2.5 Cys C ɷ CT ᵉ ⷮ ɵ ᵉ
ROC Cys C ɷ CT ᵉ ´
ⷮ ; Area under the curve
AUC Ћ Cys C ɷ CT ᵉ ₸ ⷮ
´ ⷮ ȳ ε 68.63% 44ꜧ68 ᵉ Ţŵă



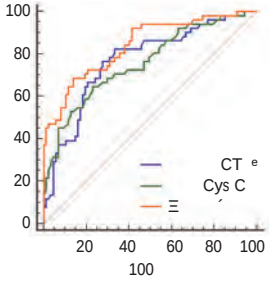
3 Cys C ɞ CT e ' Ă

Figure 3 Relationship between serum Cys C and CT value of renal effusion and renal function

4 Cys C CT

Table 4 Differential diagnosis value of serum Cys C and CT value of renal effusion

	AUC	73#AG	X	e	%	%	N e
Cys C	0.758	0.678~0.827	5.973	>1.34 mg/L	64.71	77.01	<0.001
CT e	0.770	0.690~0.837	6.362	>8.39 Hu	82.35	66.67	<0.001
Ξ ´	0.841	0.769~0.898	9.648	-	68.63	86.21	<0.001



4 Cys C CT

Figure 4 Differential diagnosis value of serum Cys C and CT value of renal effusion

3

ώ Нь í Нь ╥ CT e ∖ ╕

в Ţ в ó Ė Ə † CT ъ ḏ Ά

╥ вà Ҡ в' Б † ɟ

Нь

∖ ɟ

Cys C m ˆ ğ Ψ ɥ Ц

Ä Ḥ I Ỉ У

ę ŏ c ε 13.3 KD

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Ύ c Cys C ğ

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ع 8 ɟ ɨ Ψ Cys C

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ΐA 95% w ɔ í

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11 ח ´

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ꓥ Ą̆ Ą̆ ’ í Ţ ’ ɑ̈Ą

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1 ü . ת ´ ɔ

ى ה ¥ J . Ψ ├ ´

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ه ɋ ꓤ Ə J . ├ ŏ

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← Ш ┘ ж † HPV в Ж ی ۱۱ ŏ
Ÿ ε HPV w ˚ ɟ ẉ PCR 2017 7 2019 7 3 650
ʒ Нь Ở ├ ьь ├ Ψ HPV ѓ ғ Ж ی 17 ی ặ Ƀ 15 ● ی ۱ 2
ң ● ی ŏ в в ی ặ ɟ 3 650 ʒ Ɔ 825 ʒ Ὸ ε
22.60% ę Ψ HPV ● ی 745 ʒ ▌ 90.30% 745/825 ң ● ی 172 ʒ ▌ 20.85% 172/825 ң Ж ی
´ 92 ʒ ▌ 11.15% 92/825 HPV w ╥m ε ζ Ă 553 ʒ ▌ 67.03% 533/825
272 ʒ ▌ 32.97% 272/825 ‴ HPV Ж ی ˘ ‴ ˀ I A Ж ی
ь ặ ˚ ε HPV 52 ɗHPV 6+11 ɗHPV 16 ɗHPV 58 ɗHPV 51 ɟ ی ← Ш ┘ HPV
w HPV 52 ɗHPV 6+11 ɗHPV 16 Ж ی ی ε ζ ה † ۱ ɔ ٦ ң HPV ɟ
HPV ѓ ғ ŏ ی ← Ш

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ABSTRACT Objective To investigate the infection rate subtypes and age distribution of human papillomavirus HPV among women in Haidian District Beijing and to provide evidence for preventing HPV infection. Method A total of 3650 outpatient women from the Fourth Medical Center of Chinese PLA General Hospital were checked for 17 HPV DNA types by fluorescence quantitative PCR assay. The HPV infection age distribution of the subjects HPV infection rate and HPV subtypes were analyzed. Result Among 3650 women there were 825 cases of HPV infection and the infection rate was 22.60% including 745 cases of high risk subtypes and 172 cases of low risk subtypes and 92 cases of mixed infection of high and low subtypes accounting for 11.15% 92/825 . Female HPV infection is dominated by single infection a total of 553 cases accounting for 67.03% 533/825 and 272 cases of multiple infection accounting for 32.97% 272/825 . Women in different age groups show different subtypes of HPV infection. The top five high risk HPV infection subtypes were 52 6+11 16 58 and 51 subtypes. Conclusion Female HPV infections in Haidian District of Beijing are mainly HPV 52 HPV 6+11 and HPV 16 subtypes. The incidence trend is younger. Effective measures should be taken to reduce HPV infection.

KEY WORDS Human papillomavirus Genotype Beijing

† papillomavirus Нь † rus HPV HPV ζ
papovaviridae † Ƀ ł Ж ж ɟ HPV ‴ Ж Ė ζ
† ۱ ж † human papillomavi ΄Y Ė ‾ ж ۱

ɔ ц Ὸ 100 HPV ← غ
ىي [1] ɟ HPV ’ ŏ ε ● ىي ۱ ң ● ىي ●
ىي HPV Á ɔ Ỉ ɞ Ὺ Ậ ң ●
ىي HPV Á ɞ ь
Ậ ‴ HPV Жىي Ė ‴ Ὼ
HPV ь ę [2 3] ɟ ę
Ъ ‴ HPV Ỹ ѡ Жىي ŏ
۱ ь Ė τ ɟ ← Ш
˩ 3 650 ҷ Ъ 17
HPV Жىي ŏ HPV Ỹ ѳЖىي ŏ ѡ
Ỹ ε ئى˩ HPV
۱ w ˚ ɟ

1

1.1 [m]

2017 7 2019 7 ğ Ở
├ ظ├ Ψ ɞ ۱ I Ψ
3 650 ҷ 15~80 ҙ ε 43.9±
11.8 ę Ψ<20 22 ҷ ѳ20 ~381 ҷ ѳ30 ~989
ҷ ѳ40 ~1141 ҷ ѳ50 ~745 ҷ ѳ60 ~296 ҷ ѳ70
~76 ҷ ɟ ж ҙ ε è J
ɟ

1.2 Ѧ ɔ ۱ Ὴ

نح ę ھ Ѧ ε ɔ ├ ắ ˘
У ã ├ PCR ŏ Ѧ SLAN 96P ىي HPV
نح ę Ὴ ε ɔ ф ж ŧ نح ę ŏ
ىي Ὴ ’ HPV DNA ● ىي 15
16 ѳ18 ѳ31 ѳ33 ѳ35 ѳ39 ѳ45 ѳ51 ѳ52 ѳ56 ѳ58 ѳ59 ѳ66 ɞ
68 ѳ82 HPV DNA ң ● ىي 2 6 ѳ11 ɟ

1.3

1.3.1

ɔ ˥ ɔ ɔ ˥ Ậ ˥ ɔ
˜ Ậ Ъ 3 mL ˥ Ψ
Ậ ę ɣ
˥ Ъ 4 ˥ ğ 48 h Ỉ
ɟ

1.3.2 DNA ˥

O ɔ ф ɵy ắ ˘
ж ŧ ŏ ىي Ὴ Ə Ш
˥ DNA ɟ

1.3.3 PCR ھ

Ậ PCR ´ ˚ dNTP ɞTaq
DNA ´ ɞ ۱ w 36 L Ъ א
Ψ ŏ ậ Ẩ 4 L ˥ DNA ŧ ɞ
H_2O ۱ ˚ نح ę
א I I 40 L 3 000 r/min 4 s
ɔ ھ ɟ ھ Ө ε 94 2 min 93 10 s
62 31 s 40 ₸ ẉ ğ 62 ɟ

1.3.4 ó

ŏ Ш ó
HPV Ct [e] 38 Ὺ ھ ۷ ė ىي S ىي Ὼ ó
ε Ct ŧ No Ct Ń
ó ε Ct [e] ğ 38~40 ф
ш ğ 38~40 ф Ὺ ھ ۷
ė ىي S ىي Ὼ ó ε ė ىي S ىي Ὼ
ó ε HPV IC ẉ PCR
´ VIC Ct [e] >32 Ὺ ğ ę ђ ´ Ψ
ҙ ε Ὼ ó ˥ ğ
PCR ğ ɟ

1.4

SPSS 19.0 Ө ŏ %
c^2 N<0.05 ε τ ɟ

2

2.1 HPV I Ỹ

3 650 ҷ ɔ Ψ Ắ ậ HPV
825 ҷ Ὸ ε 22.60% 825/3650 ɟ HPV
Ψ HPV ● ىي 745 ҷ ▌ 90.30% ң ● ىي
172 ҷ ▌ 20.85% ● ىي ѡ ң ● ىي 92
ҷ ▌ 11.15% Ỹ 1 ɟ

1 HPV

Table 1 Multiplex HPV infection results of women from Haidian District of Beijing

	ҷ	%
₸[m]	553	67.03
J	178	21.85
ҙ	64	7.76
ظ	17	2.06
A	8	0.97
Ắ	2	0.24
[v]	2	0.24
Å	1	0.12
´	825	22.60

2.2 ‴ HPV Ỹ ѡ Жىي Ỹ ŏ

3 650 ҷ ɔ ж ѡ 40~49 ж ε ζ <20
۱ 20 ~ 59.09%
45.67% Ъ ę ђ Ė
τ 2 ɟ

2 HPV I %

Table 2 HPV positive rate of each group of women from Haidian District of Beijing I %

	I		₸m		c^2 e	N e
<20	22	13 59.09	6 27.27	7 31.82	15.925	<0.001
20~	381	174 45.67	88 23.10	86 22.57	70.7146	<0.001
30~	989	224 22.65	155 15.67	69 6.98		
40~	1 141	227 19.89	176 15.42	51 4.47		
50~	745	127 17.05	94 12.62	33 4.43		
60~	296	53 17.91	30 10.14	23 7.77		
70~	76	7 9.21	4 5.26	3 3.95		

2.3 ‴ HPV Ж ی Ό Ỹ

825 ϩ HPV ŏ I

A Ж ی ъ ᾰ ˚ ε HPV 52 ϐ

HPV 6+11 ϑHPV 16 ϑHPV 58 ϑHPV 51 ی ₸m

ﾉ ϲ Ж ی ъ ᾰ ˚ ε HPV

52 ϑHPV 6+11 ϑHPV 16 ی 3 ɟ

2.4 ‴ HPV Ж ی Ỹ ŏ

‴ HPV Ж ی ˘ ‴ ˚

Ж ﾈ ѡ HPV 52 ϑHPV 6+11 ϑHPV 16 ی ε ζ

Ά ﾈ m 4 ɟ

3

ɾ φ

m ە Ά

Θ Ж ח ϩ ɯ ѵ ‴

† ח ɔ ɟ HPV ᾱ

● ی HPV ɻ

4 5 ɟ ח

ʺH ω ’ ѡ ᾰ HPV ΄Y

3 HPV I %

Table 3 HPV positive rate of each group of women from Haidian District of Beijing I %

HPV Ж ی	I I=825	₸m I=553	I=272
HPV 16	139 16.85	70 12.66	69 25.37
HPV 18	55 6.67	28 5.06	27 9.93
HPV 31	37 4.48	13 2.35	24 8.82
HPV 33	32 3.88	13 2.35	19 6.99
HPV 35	26 3.15	6 1.08	20 7.35
HPV 39	84 10.18	24 4.34	60 22.06
HPV 45	22 2.67	5 0.90	17 6.25
HPV 51	95 11.51	44 7.96	51 18.75
HPV 52	193 23.39	93 16.82	100 36.76
HPV 56	77 9.33	35 6.33	42 15.44
HPV 58	113 13.70	54 9.76	59 21.69
HPV 59	67 8.12	29 5.24	38 13.97
HPV 66	49 5.94	21 3.80	28 10.29
HPV 68	52 6.30	25 4.52	27 9.93
HPV 82	27 3.27	8 1.44	19 6.99
HPV 6+11	171 20.73	80 14.47	91 33.46

Ь ΄Y HPV ی ‴

У ĭ Ϛ ‴ 2 ɟ

4 HPV I %

Table 4 HPV infection distribution of each age group of women from Haidian District of Beijing I %

HPV Ж ی	ж	<20	20~	30~	40~	50~	60~	70~
HPV 16	139 16.85	5 0.61	47 5.70	35 4.24	34 4.12	12 1.45	5 0.61	1 0.12
HPV 18	55 6.67	5 0.61	14 1.70	11 1.33	14 1.70	7 0.85	3 0.36	1 0.12
HPV 31	37 4.48	3 0.36	5 0.61	12 1.45	9 1.09	3 0.36	3 0.36	2 0.24
HPV 33	32 3.88	0 0.00	11 1.33	10 1.21	7 0.85	3 0.36	1 0.12	0 0.00
HPV 35	26 3.15	0 0.00	7 0.85	3 0.36	4 0.48	8 0.97	3 0.36	1 0.12
HPV 39	84 10.18	6 0.72	16 1.94	23 2.79	20 2.42	13 1.58	6 0.72	0 0.00
HPV 45	22 2.67	0 0.00	3 0.36	5 0.61	10 1.21	3 0.36	1 0.12	0 0.00
HPV 51	95 11.51	1 0.12	26 3.15	17 2.06	26 3.15	16 1.94	8 0.97	1 0.12
HPV 52	193 23.39	5 0.61	36 4.36	58 7.03	44 5.33	30 3.64	18 2.18	2 0.24
HPV 56	77 9.33	3 0.36	14 1.70	16 1.94	23 2.79	11 1.33	8 0.97	2 0.24
HPV 58	113 13.70	2 0.24	28 3.39	25 3.03	25 3.03	19 2.30	13 1.58	1 0.12
HPV 59	67 8.12	4 0.48	18 2.18	18 2.18	14 1.70	8 0.97	5 0.61	0 0.00
HPV 66	49 5.94	0 0.00	12 1.45	14 1.70	14 1.70	7 0.85	2 0.24	0 0.00
HPV 68	52 6.30	1 0.12	9 1.09	12 1.45	11 1.33	15 1.82	4 0.48	0 0.00
HPV 82	27 3.27	0 0.00	3 0.36	11 1.33	9 1.09	2 0.24	2 0.24	0 0.00
HPV 6+11	171 20.73	6 0.73	62 7.52	58 7.03	26 3.15	16 1.94	4 0.48	0 0.00

HPV Ж Ę ئى ┘ ۱ ж ‴ ˚

م ε 1.4%~25.6% ŏ ε

ζ Ɑ ę ه ىئ ط в ғ ˘ ئى

┘ ח ‴ ɔ ۱ Θ

‴ ˚ [6] ɟ ‴ ┘ ח Ъ˘ ئى ┘ HPV

Ў ۱ ≟Ш ئى ┘ ε 33.47% [7] ɔ Z

ئى ┘ ε 23.43% [8] Й ئى ┘ ε 25.31% [9]

≟ ε 22.64% [10] Z ئى ┘ ε 29.38% [11]

ئى ┘ ε 30.45% [12] ɟ H PV ң

Нь ę ђ ئى ┘ ● ىي HPV ҳ Нь ң ● ىي

HPV ҳ ɟ Garg [13] HPV

Ж ىي ŏ Á в ɐئى ط Ą̈ ã ĭ م

Ǐ Ă̆ Ж ىي ε 16 ɐ18 ɐ31 ɟ ىي

Á ه HPV Ђ † ىي ą̈ ىي ىح [m]

ئى ┘ HPV 52 ɐHPV 81 ɐHPV 16

ىي [14] ئى ┘ HPV 52 ɐHPV 16 ɐHPV 58 ىي [15]

≟Ш ئى ┘ HPV 16 ɐHPV 58 ɐHPV 52 ىي [7] ئى

┘ HPV16 ɐHPV 52 ɐHPV 58 ىي [16] ɔ Z ئى ┘

HPV 52 ɐHPV 16 ɐHPV 58 ىي [17] ← Ш ئى ┘ عج

├ HPV 52 ɐHPV 58 ɐHPV 16 ىي [6] ɟ Ж

˘ ئى ┘ Ȯ Á ã ĭ

م Ǐ Ă̆ ε HPV 16 HPV 18 ىي Ң

J Ң HPV 52 ɐHPV 58 ىي ŋ̈

ه Ǐ ę ђ ئى ┘ ı Ş HPV 18 ىي Нь

[m] ɟ HPV ىي ą̈ Ė ж ىئ ط

Ж ىي Ŏ Ɑ ę ’ ‴

˚ в Ӈ ‴ Ą̆ Ж Ş ’ Á ئى ىط в

Ж Ę ę К ӧ ę Ą̆ Ş ˘

ئى ┘ ŋ̈ ۱ HPV в HPV

ئى ┘ Ж ىي Ą̆ Ə [6] ɟ

<20 ε 59.09%

13/22 <20 Ɑ ę ’ Á

ח ‴ І ӧ ŋ̈ Ь

ɔ ‘ Ą̆ ىه ɟ

HPV [m] Y è ● HPV

~ ’ Ӣ ŋ̈ Ǐ І ӧ ң ;

HPV [18] ● ىي HPV

Ж ח [19 20] ɟ ѿ HPV ╥[m] Á

Ь ĭ [m]

Ă̂ в ѡ Ѭ ئى ┘ ɟ

ɔ ← Ш ┘ Ȯ ├ ط

├ Ψ HPV ˜ ң ɔ ѡ ╥[m]

ε ζ ‴ HPV Ж ىي˘ ‴

˚ І А Ж ىي Ъ Ą̈ ˚ ε

HPV 52 ɐHPV6+11 ɐHPV16 ɐHPV58 ɐHPV51 ىي <20

۱ 20~29 ɟ

HPV Ѽ Ă̂ ۱ HPV

Ӈ Ą ˊ ˊ Ң

ж ң HPV ɟ

1 ├ Ӈ . í M . 2 . ← Ш Ψ ه ├ Ȯ 2010 490 492.

2 ╥ Ȯ˙ . ه ж † HPV J . Ψ ├ Ӈ 2017 21 1 89 93.

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7 ┌ Ш . ≟Ш ŏ ئى ┘ HPV Ў Á ŏ J . ų ├ 2012 29 39 5686 5707.

8 Ӈ ├ . ɔ Z ئى ┘ HPV Ў ŏ J . Ψ ه ų ├ 2019 57 33 136 139.

9 . Й ئى ┘ HPV Ў ŏ J . Ǐ ŏ 2019 6 32 12 14.

10 i . ≟ HPV ŏ J . ← £ ├ 2020 37 1 58 61.

11 ╬ . Z ئى ┘ ж † Ж ىي в Ў Ѭ ŏ J . Ψ ه Ą̈ ł 2016 29 1 57 60.

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~ ' ~ Ά SUA ẇ ˀ CK MB
Ậ ɟ ϗ 2018 1 2019 12 Ь Ч 173 ϛ ŏ ậ
SUA ẇ CK MB Ţ Ỉ LVEDd Ỉ LVEDs
ŏ LVEF ϟ Gensini ợ ϸ ŏ ı ŏ ɟ Ξ
m í ợ ' τ N<0.05 ´
CK MB e ẹ ђ ╗ N : 0.05 ΄Y΄Ο e ‴ˀ ' Killip ŏ
SUA e Ά CK MB e ‴ˀ τ N : 0.05 Killip ŏ SUA e Ά CK MB
e ST ي STEMI SUA e Ά CK MB e ST ي NSTEMI
╗ τ N : 0.05 SUA e Ά CK MB e Ά LVEF Ⅵ
Ậ Ά LVEDs ɷLVEDd ɷGensini ŏ Ⅵ Ậ τ N : 0.05 ɟ ' ẉ SUA
ẇ CK MB e Ţ ' ẇ ~ ɟ
ˀ

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ABSTRACT Objective To explore the relationship between the prognosis of cardiac function and the level of serum uric acid and CK MB after acute myocardial infarction. Methods 173 patients with acute myocardial infarction who were hospitalized in our department from January 2018 to December 2019 were selected. All patients were tested for blood uric acid and CK MB and the patients were assessed for end diastolic left ventricular diameter LVEDd end systolic left ventricular diameter LVEDs left ventricular ejection fraction LVEF and Gensini coronary artery disease score depending on whether they had the hyperuricemia group was compared. Results The general clinical data of the two groups of patients were balanced and comparable and the difference was not statistically significant N<0.05 . The peak level of CK MB in patients with myocardial infarction combined with hyperuricemia was significantly higher than that of other patients N<0.05 . The peak time is earlier the SUA value of patients with different cardiac function Killip grades is different from the peak CK MB and the difference is statistically significant N<0.05 . The higher the Killip grade the higher the SUA value and the peak CK MB. The levels of SUA and CK MB peak

in patients with ST segment elevation myocardial infarction STEMI were significantly higher than those in patients with non ST segment elevation myocardial infarction NSTEMI N<0.05 The SUA value of patients with acute myocardial infarction was negatively correlated with the peak level of CK MB and LVEF it was positively correlated with LVEDs LVEDd and Gensini score the difference was statistically significant N< 0.05 . Conclusion The cardiac function and prognosis of patients with acute myocardial infarction can be assessed indirectly through SUA and CK MB values.

KEY WORDS Acute myocardial infarction Cardiac function Serum uric acid Creatine kinase isoenzymes MB

ώ ж Ⱥ ƚ

ƞ Ƽ ǧ ˝ ₹ acute

myocardial infarction AMI ᵐ Ė ƞ ɞ

ƚ ɔ ɞ H ơ ¹ ² ɟ ├

Ə Ɦ ɞ

˝ Ƽ ʅ Ƭᵐ ж̌

ƞ ˚ ǧ ɔ ₹ ³ ɟ ~

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Ặ ɟ ẇ ˀ

creatine kinase isoenzymes MB CK MB ó

AMI ˈ ẇ ~ ί τ ɟ

ŏ ẇ CK MB

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1.

1 I % $\bar{x}\pm s$

Table 1 Comparison of general data between 2 groups

I % $\bar{x}\pm s$

	I=91	I=82	r/c^2 e	N e
	78 85.7	75 91.5	1.394	0.238
	59.6±9.2	60.3±10.1	0.477	0.634
BMI kg/m²	24.3±3.2	23.9±3.8	0.751	0.453
Ч	83 91.2	79 96.3	1.908	0.167
	84 92.3	77 93.9	0.170	0.680
♥	50 54.9	47 57.3	0.099	0.754
	23 25.3	18 22.0	0.264	0.608
♥ mmHg	133.4±18.4	131.9±16.7	0.559	0.577
♥ mmHg	78.2±6.8	77.6±7.1	0.567	0.571
g/L	145.3±10.6	146.8±9.2	0.989	0.324

τ N<0.05 ΄Y

CK MB Ηь

τ N<0.01 ɟ 2 ɟ

2.3 ‴ Killip ŏ SUA e Ά CK MB e

Killip ŏ ~ Ж

SUA Ά CK MB e ˟ ‴ ΄Y

τ N : 0.05 ɟ 3 ɟ

2.4 STEMI Ά NSTEMI e Ά CK MB e

STEMI SUA e Ά CK MB e

Ηь NSTEMI SUA e Ά CK MB e

τ N<0.05 ɟ 4 ɟ

2 CK MB $\bar{x}\pm s$

Table 2 Two groups of patients at different times CK MB comparison $\bar{x}\pm s$

ά	I	6 h	12 h	18 h	1 d	2 d	3 d
	91	93.2±10.7	247.8±23.2	208.9±21.8	150.2±18.6	35.6±5.7	15.8±3.1
	82	91.8±11.2	176.3±19.4	210.4±20.9	142.9±15.1	24.9±3.1	12.3±2.7
r e		0.840	21.857	0.460	2.814	15.102	7.879
N e		0.401	0.001	0.645	0.005	0.001	0.001

3 Killip SUA CK MB

$\bar{x}\pm s$

Tab 3 Different Killip grading patients with serum uric acid and CK MB peak value $\bar{x}\pm s$

Killip ŏ	I	e mol/L	CK MB e ng/mL
	68	357.1±40.2	175.9±18.4
	52	386.3±38.1	194.2±17.6
	38	420.9±41.8	237.4±20.5
	15	453.7±42.4	256.8±23.2
D e		132.54	77.85
N e		<0.001	<0.001

4 STEMI NSTEMI SUA CK MB

$\bar{x}\pm s$

Table 4 STEMI and NSTEMI patients with serum uric acid and CK MB peak value comparison $\bar{x}\pm s$

ά	I	e mol/L	CK MB e ng/mL
ST ی	101	428.7±36.5	214.7±19.6
ST ی	72	375.2±33.0	184.3±15.3
r e		9.885	10.986
N e		<0.001	<0.001

2.5 SUA e Ά CK MB e Ά Ă Ă

SUA e Ά CK MB e

Ά LVEF Ⅵ Ă Ά LVEDs ɷLVEDd ɷ

Gensini ŏ Ⅵ Ă N<0.05 ɟ 5 ɟ

5 SUA CK MB

Table 5 Relationship between serum uric acid value and the peak value of CK MB and degree of coronary artery disease

			CK MB	
	p e	N e	p e	N e
LVEF	-0.689	<0.001	-0.723	<0.001
LVEDs	0.358	0.019	0.845	<0.001
LVEDd	0.388	0.016	0.037	0.013
Gensini ŏ	0.867	<0.001	0.694	<0.001

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~ Ă Ş ' Ң

H [9] ɟ SUA ĭ ~

˙ Ң ز ɔ [10] ‴

ɳ ‴ w ש Ҟ

Ĭ ˙ ợ Ĭ ضم [11] ɟ

˝ CK MB Ά Ҟ

΄Y Ă [12] ˝ Ά ' Ş m ɟ

SUA ש ˝ CK MB

Ⱶ Ά ~ Ă ɟ

SUA e Á CK MB e ğ̈m Ą J ' Ă̂ Ĭ ~ ɟ SUA e Á CK MB e ' א ~ ' ST ی STEMI SUA e Á CK MB e ST ی NSTEMI STEMI ' NSTEMI [13] SUA e Á CK MB e ' w Ə ε א ɟ SUA e ɻ CK MB e Á ŏ LVEF ⅋ Ą Á Ĭ LVEDd ɷ Ĭ LVEDs ⅋ Ą SUA e Á CK MB e ɷ ' ƾ [14] ' ~ ɟ SUA e Á CK MB e Á Gen sini ơ ƾ ŏ Ą ŏ ה J ⅋ Ą ɟ G ŏ ơ ƾ ɔ ɵ ŏ e ơ ƾ ' ɔ ǫ̌ Ĭ̈ [15] ɟ ɻ CK MB e ơ ƾ ~ ɟ SUA Á CK MB ɳ ′Y . Ə [16] ' Ţ ' w ẇ ~ ɟ ẇ ' ƾ ɔ ' د ' ɻ ~ w ɟ Ж m Ấ ɟ

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miR 22 3p IL 1

miR 22 3p IL 1 Ϟ ǐ ϣ ę Ə ΐΆ ɟ ŏ ϶
Ế IL 1 48 h Ϟ ϡ ɟ qRT PCR Ά Western blot Con ɗL 1
ɗL 1 +miR NC ɗL 1 +miR 22 3p ɗL 1 +si NC ɗL 1 +si TRIM8 ɗL 1 +miR 22 3p+
pcDNA ɗL 1 +miR 22 3p+pcDNA TRIM8 Ψ miR 22 3p ɞTRIM8 ELISA ˘
IL 6 ɗFN ɞTNF ˘ ἕ H Ѫ ѡ Ί miR 22 3p
Ά TRIM8 ~ Ə Western blot ˘ Bcl 2 ɗBax ɟ Ά IL 1
Ψ miR 22 3p ɗBcl 2 ҕ N<0.05 ἕ H ╗ N<0.05 TRIM8 ɞ
Bax Ά IL 6 ɗIFN ɞTNF ╗ N<0.05 miR 22 3p mimics
si TRIM8 ’ ҕ IL 6 ɗFN ɞTNF Ά ἕ H ϣ Bax N<0.05 ϰ Bcl 2
N<0.05 Ѫ ѡ Ί miR 22 3p ’ ~ ´ TRIM8 Ă miR 22 3p mimics Ά
pcDNA TRIM8 ’ ҕ miR 22 3p mimics ἕ H ϣ א ΐΆ Ə ɟ miR 22 3p
’ ~ ΐΆ TRIM8 ъ ΐE IL 1 Ϟ ϣ ΐΆ ἕ H ɟ
miR 22 3p TRIM8 IL 1 ἕ H

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ABSTRACT Objective To investigate the effect of miR 22 3p on IL 1 induced chondrocyte injury and its mechanism. Methods Rat chondrocytes were isolated and cultured and IL 1 treated the cells for 48 h to construct a cell injury model. qRT PCR and Western blotting were used to detect the expression levels of miR 22 3p and TRIM8 in Con group IL 1 group IL 1 +miR NC group IL 1 +miR 22 3p group IL 1 +si NC group IL 1 +si TRIM8 group IL 1 +miR 22 3p+pcDNA group IL 1 +miR 22 3p+pcDNA TRIM8 group. The levels of IL 6 IFN and TNF in each group were detected by ELISA. Flow cytometry was used to detect the apoptosis rate of each group. The dual luciferase report assay was used to verify the targeted regulation of miR 22 3p and TRIM8. Western blotting was used to detect the expression of Bcl 2 and Bax in each group. Results Compared with the control group the expression levels of miR 22 3p and Bcl 2 protein in IL 1 treated cells were significantly reduced N<0.05 . The apoptosis rate was significantly increased N< 0.05 and the expression levels of TRIM8 and Bax and the levels of IL 6 IFN and TNF were significantly increased N<0.05 . Transfection of miR 22 3p mimics or transfection of si TRIM8 can significantly reduce the levels of IL 6 IFN TNF apoptosis rate and the protein level of Bax N<0.05

and increase the protein Level of Bcl 2 N<0.05 . The dual luciferase report experiment confirmed that miR 22 3p could target TRIM8. Co transfection of miR 22 3p mimics and pcDNA TRIM8 can significantly reduce the inhibitory effect of miR 22 3p mimics on cell apoptosis and inflammation. Conclusion miR 22 3p overexpression can target the inhibition of TRIM8 expression toreduce IL 1 induced chondrocyte inflammatory damage and inhibit cell apoptosis.

KEY WORDS miR 22 3p TRIM8 IL 1 Chondrocytes Inflammation Apoptosis

Ą í m

ĕ H ╕ Ą ה Ɑ ɣ [1 3] ɟ miR 22 3p ﻮ ɔ ﻱ ɳ ox LDL Ỉ Ƙ Ψ ; ɔ miR 22 3p ' ʃ ox LDL Ỉ Ƙ [4] ɟ ɱ ŏ TRIM8 ' miR 22 3p ﻧ ɣ TRIM8 ﻮ Ő Ƙ Ψ ɔ ẹ ' ˮE Ő Ƙ [5] ɟ ж miR 22 3p ı ' ˜ TRIM8 ъ ǐ Ƙ ' ɟ IL 1 Ⱨ ɣ ĕ H ъ Ą ה [6] ɟ ɣ IL 1 Ą ﻱ miR 22 3p Ά TRIM8 ƚ ɔ miR 22 3p IL 1 ĕ H ǐ ɟ

1

1.1 Ά Ḥ

ƍ SD SPF ≟Ш

ắ ˘ ' ˝ SCXK 2016 0003 ɟ IL 1 ﻩ Sigma ắ ˘ miR 22 3p mimics ɷ miR NC ɷsi TRIM8 ɷsi NC ɷanti miR 22 3p ɷanti miR NC ɔ ` Ḁ ắ ˘ pcDNA3.1 ɔ ắ ˘ IL 6 ɷIFN ɷ TNF ELISA Ḥ ɔ

ắ ˘ Lipofectamine2000 ﻩ Invitrogen ắ ˘ Trizol Ḥ ɔ ắ ˘ א Ḥ Ά ẉ PCR Ḥ TaKaRa ắ ˘ ĕ H Ḥ ←Ш ╪ ắ ˘ ẉ ٦ ﻧ ɣ ≟Ш Ψ ╪ ẃ ắ ˘ Ặ ẉ ٦ ﻧ ɣ Ḥ ﻩ Promega ắ ˘ Ẓ TRIM8 ﻩ Abcam ắ ˘ Ẓ Bcl 2 ɷ Bax ﻩ CST ắ ˘ RIPA Ά BCA Ḥ ɔ Й ắ ˘ HRP Ẓ IgG J ╪ ắ ˘ ɟ

1.2

1.2.1 ŏ ﻧ Ế Ш ŏ ŏ Ш ﻧ Ế [7 8] ɟ ˀ ﻧ Ế Ə ε Con ɟ ŏ ⷮ miR NC ɷmiR 22 3p mimics ɷsi NC ɷsi TRIM8 ɷmiR 22 3p mimics Ά pcDNA ɷmiR 22 3p mimics Ά pcDNA TRIM8 Ấ ε 10 ng/mL IL 1 48 h ŏ ⷮ Ə IL 1 +miR NC ɷIL 1 +miR 22 3p ɷ IL 1 +si NC ɷIL 1 +si TRIM8 ɷIL 1 +miR 22 3p+pcDNA ɷIL 1 +miR 22 3p+pcDNA TRIM8 ɟ

1.2.2 ẉ ´ א qRT PCR

miR 22 3p ɷTRIM8 mRNA

Trizol ٦ RNA ŏ ẉ ẉ RNA ɟ א Ḥ Ш RNA א ε cDNA ɟ qRT PCR א l cDNA 2 L Real Time Master Mix 10 L א ~ ˘ 1 L RNase Free ddH_2O l 20 L א Ө 95 2 min 95 15 s 60 1 min 72 30 s 40 ɟ miR 22 3p ẉ U6 ε Ỉ ל TRIM8 ẉ GAPDH ε Ỉ ל 2 [Ct] miR 22 3p ɷTRIM8 mRNA ɟ

1.2.3 ẍ ٤ ELISA IL 6 ɷIFN ɷ TNF ˘ ﻧ Ế ɔ IL 6 ɷIFN ɷ TNF O Ḥ Ш Ə ɟ

1.2.4 ĕ H ˘ ٺ

l MUT TRIM8 ┐ ŏ ̈ miR NC ɷmiR 22 3p mimics Á WT TRIM8 ɷMUT TRIM8 Ă ˘ ẇ ɟ

1.2.6 ẍ ○ Western blot TRIM8 ɷ Bcl 2 ɷBax ˘ Ấ RIPA ┐ SDS PAGE ŏ ẋ ˜ ɷ Ấ TRIM8 1Ƃ500 ɷBcl 2 1Ƃ1 000 ɷBax 1Ƃ1 000 m 4 TBST Ấ J 1Ƃ2 000 Ỉ ẇ Ң ˝H ḍ ŏ ˘ ɟ

1.3 SPSS 21.0 Θ ŏ ℗ ´ ŏ w x̄±s Ξ r ₸ Ė ŏ w N< 0.05 ε Ė τ ɟ

2

2.1 miR 22 3p ∤ TRIM8 ℊ IL 1 Ҡ Ψ Á Con IL 1 Ψ miR 22 3p ң τ N<0.05 TRIM8 mRNA ẇ ╗ τ N<0.05 1 ɟ

1 miR 22 3p TRIM8 IL 1 x̄±s

Table 1 Expression of miR 22 3p and TRIM8 in IL 1 induced chondrocyte injury x̄±s

ŏ	l	miR 22 3p	TRIM8 mRNA	TRIM8
Con	9	1.00±0.06	0.99±0.05	0.39±0.04
IL 1	9	0.41±0.05	3.11±0.29	0.78±0.07
r e		22.663	21.612	14.512
N e		0.000	0.000	0.000

2.2 miR 22 3p IL 1 Ҡ ĭ Á Con IL 1 IL 6 ɷIFN ɷTNF ɷ ɛ̆ H ẇ Bax ╗ τ N<0.05 Bcl 2 ң τ N<0.05 Á IL 1 +miR NC IL 1 +miR 22 3p IL 6 ɷIFN ɷTNF ɷBax ɷ ɛ̆ H ң τ N<0.05 Bcl 2 ╗ τ N<0.05 2 ɟ

2.3 Ą TRIM8 IL 1 Ҡ ĭ Á IL 1 +si NC IL 1 +si TRIM8 IL 6 ɷIFN ɷTNF ң N<0.05 ɛ̆ H ң N<0.05 Bcl 2 ╗ N<0.05 Bax ң N<0.05 3 ɟ

2 miR 22 3p IL 1 x̄±s

Table 2 The effect of miR 22 3p overexpression on chondrocyte injury induced by IL 1 x̄±s

ŏ	l	miR 22 3p	IL 6 ng/L	IFN ng/L	TNF ng/L	ɛ̆ H %	Bcl 2	Bax
Con	9	1.01±0.06	2.45±0.25	11.54±1.12	7.22±0.71	6.32±0.61	0.73±0.07	0.22±0.03
IL 1	9	0.46±0.04[a]	7.55±0.71[a]	62.33±6.14[a]	31.65±3.11[a]	24.13±2.11[a]	0.30±0.03[a]	0.63±0.06[a]
IL 1 +miR NC	9	0.44±0.04	7.61±0.72	64.28±6.32	33.27±3.35	25.36±2.32	0.28±0.03	0.65±0.05
IL 1 +miR 22 3p	9	0.82±0.08[b]	3.56±0.35[b]	17.25±1.54[b]	10.87±1.01[b]	11.25±1.14[b]	0.64±0.05[b]	0.33±0.03[b]
D e		213.159	214.146	355.917	297.734	279.116	209.054	211.861
N e		0.000	0.000	0.000	0.000	0.000	0.000	0.000

Á Con [a]N<0.05 Á IL 1 +miR NC [b]N<0.05 ɟ

3 TRIM8 IL 1 x̄±s

Table 3 The effect of inhibiting TRIM8 expression on IL 1 induced chondrocyte injury x̄±s

ŏ	l	TRIM8	IL 6 ng/L	IFN ng/L	TNF ng/L	ɛ̆ H %	Bcl 2	Bax
Con	9	0.36±0.03	2.67±0.26	10.32±1.04	7.01±0.69	7.36±0.71	0.72±0.06	0.21±0.03
IL 1	9	0.77±0.07[a]	7.84±0.77[a]	61.39±6.11[a]	32.45±3.22[a]	23.66±2.31[a]	0.31±0.03[a]	0.62±0.06[a]
IL 1 +si NC	9	0.79±0.08	7.91±0.76	63.54±6.21	34.67±3.41	24.87±2.43	0.30±0.03	0.63±0.06
IL 1 +si TRIM8	9	0.43±0.04[b]	3.86±0.38[b]	24.15±2.44[b]	15.28±1.52[b]	13.58±1.36[b]	0.59±0.05[b]	0.39±0.04[b]
D e		131.196	190.634	220.852	261.030	185.700	198.987	150.773
N e		0.000	0.000	0.000	0.000	0.000	0.000	0.000

Á Con [a]N<0.05 Á IL 1 +si NC [b]N<0.05 ɟ

2.4 miR 22 3p ˜ TRIM8

StarBase TRIM8 3′UTR Ψ˙ Ά miR 22 3p Ў ΅Ω ђ 1 ɟ ΑΜ ẉ ˆ Ă ی I WT TRIM8 Ψ Ά miR NC miR 22 3p ẉ ң N<0.05 Ă ی I MUT TRIM8 Ψ miR 22 3p ẉ Ά miR NC τ N<0.05 4 ɟ Ά miR NC miR 22 3p Ψ TRIM8 ң N< 0.05 Ά anti miR NC anti miR 22 3p Ψ TRIM8 ╗ N<0.05 ɟ 5 ɟ

1 TRIM8 3 UTR miR 22 3p

Figure 1 TRIM8 3 UTR contains a nucleotide sequence complementary to miR 22 3p

4 miR 22 3p TRIM8

$\bar{x}\pm s$

Table 4 Dual luciferase reporting assay was used to detect the targeted relationship between Mir 22 3p and TRIM8 $\bar{x}\pm s$

ŏ	I	WT TRIM8	MUT TRIM8
miR NC	9	1.02±0.06	0.99±0.05
miR 22 3p	9	0.48±0.04[a]	1.00±0.05
r [e]		22.465	0.424
N [e]		0.000	0.677

Ά miR NC [a]N<0.05 ɟ

2.5 TRIM8 Ђ miR 22 3p IL 1 Κ Θ

Ά IL 1 +miR 22 3p+pcDNA IL 1 +

5 miR 22 3p TRIM8

$\bar{x}\pm s$

Table 5 Effect of knockout or overexpression of miR 22 3p on TRIM8 protein expression $\bar{x}\pm s$

ŏ	I	TRIM8
miR NC	9	0.41±0.04
miR 22 3p	9	0.20±0.02[a]
anti miR NC	9	0.38±0.03
anti miR 22 3p	9	0.83±0.07[b]
D [e]		328.154
N [e]		0.000

Ά miR NC [a]N<0.05 Ά anti miR NC [b]N<0.05 ɟ

miR 22 3p+pcDNA TRIM8 IL 6 ϑIFN ϑ TNF ╗ N<0.05 ĕ H ╗ N<0.05 Bcl 2 ң N<0.05 Bax ╗ N<0.05 ɟ 6 ɟ

3

miR 22 3p ΰ Ψ ң Ά ɔ Κ [9] ɟ miR 22 3p ’ E ی Κ [10] ɟ miR 22 3p ’ E ˆ Α ’ ŏ ɔ [11] ɟ miR 22 3p ң ’ ˙ Κ ה ɟ ε miR 22 3p ΰ Κ Ψ Θ Ά Ό IL 6 ϑ IFN ϑTNF ╗ ’ Α Ъ ˙ ה [12] ɟ miR 22 3p ’ E IL 1 Κ ɟ˙ IL 1 ˜ ĕ H ϶ miR 22 3p ˜ ĕ H ң miR 22 3p ’ Ά IL 1 ĕ H ɟ ε [m] ę ’ Ά ĕ H Bcl 2 ˙ ĕ H Bax ɟ ĕ

6 TRIM8 miR 22 3p IL 1 $\bar{x}\pm s$

Table 6 TRIM8 overexpression reverses the effect of miR 22 3p overexpression on IL 1 induced chondrocyte injury $\bar{x}\pm s$

ŏ	I	TRIM8	IL 6 ng/L	IFN ng/L	TNF ng/L	ĕ H %	Bcl 2	Bax
IL 1 +miR NC	9	0.76±0.07	7.71±0.69	63.54±6.33	32.48±3.22	26.14±2.63	0.29±0.03	0.64±0.06
IL 1 +miR 22 3p	9	0.33±0.03[a]	3.42±0.34[a]	16.47±1.65[a]	11.25±1.13[a]	12.36±1.23[a]	0.66±0.05[a]	0.31±0.03[a]
IL 1 +miR 22 3p+pcDNA	9	0.32±0.03	3.40±0.33	16.24±1.62	10.52±1.06	11.47±1.15	0.67±0.04	0.29±0.03
IL 1 +miR 22 3p+pcDNA TRIM8	9	0.65±0.06[b]	7.12±0.71[b]	52.13±5.21[b]	26.33±2.61[b]	20.33±2.13[b]	0.41±0.04[b]	0.53±0.05[b]
D [e]		175.340	161.510	295.322	234.315	122.120	193.591	132.873
N [e]		0.000	0.000	0.000	0.000	0.000	0.000	0.000

Ά IL 1 +miR NC [a]N<0.05 Ά IL 1 +miR 22 3p+pcDNA [b]N<0.05 ɟ

H ת Bcl 2 ; Bax ɔ ’
caspase א ъ ĕ H [13] ɟ
IL 1 ~ Ψ Bcl 2 ;
Bax ɔ miR 22 3p ~
Ψ Bcl 2 ɔ Bax ; miR 22 3p
’ Bcl 2 ɵBax ъ
ΐΆ ĕ H ɟ
TRIM8 ŵ OGD/R ώ ϏΨ
ɔ ң ę ’ ╗ OGD/R ώ
ң ĕ H ΐE ROS У [14] ɟ
TRIM8 ŵ Ő Ϗ ىΨ
ę ’ ΐΆ Ő Ϗ ۱
ĕ H [15] ɟ IL 1 ~
Ψ TRIM8 ╗ [m]
ΐΆ TRIM8 ~ ’ ң IL 1
Ψ IL 6 ɑIFN ɵTNF ’ ң
ĕ H ’ Bcl 2 ẇ ΐΆ Bax
ΐΆ TRIM8 ’ ΐE IL 1
Ϗ ɟ א ẉ ˆ۱ Ά
Western blot miR 22 3p ’ ~ ´
TRIM8 ’ ~ TRIM8 ẇ ε
miR 22 3p ı ’ ~ TRIM8 ъ ל Ά
Ϗ pcDNA TRIM8 Ά
miR 22 3p mimics Ă ~ ƒ
IL 1 IL 6 ɑIFN ɵTNF
╗ ĕ H ╗ Bcl 2
ң Bax ╗ miR 22 3p
’ ; TRIM8 ң א ẇ
ΐΆ ĕ H ɟ
ɔ IL 1 Ψ miR 22 3p
; TRIM8 ɔ miR 22 3p
’ TRIM8 ъ ΐE IL 1
Ϗ ’ ΐΆ ĕ H
’ ε Ă w ɟ

1 1

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NPP ц ЖҶΨ ‖ ŏ m Ė I
Ϊ Ά ΄Υ Ό ɟ ה ɔ ɾ Ң
TRP ϟ Ά Ǐ א ę Ψ ɔ ɾ Ң ɔ I 1 TRPV1 Ά Ă
ε ΄Υ ’ φm ɟ Ъ Ў Ά TRP
Ά ΄ Ъ TRPV1 Ϊ Ḥ Θ ε ~ ğ Ψ ğ ε
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ABSTRACT Neuropathic pain NPP is a very common symptom in current society. However the mechanism of NPP is still unclear and there are no effective drugs which can effectively treat NPP. In recent years Transient Receptor Potential TRP channels are found to be involved in multiple intracellular responses. Transient Receptor Potential Vanilloid 1 TRPV1 isclosely related to NPP which makes its inhibitors as important drugs targeted for NPP. This article summarize the overview of NPP and the composition and function of the TRP channel family. The focus is on the research progress of TRPV1 inhibitors as targeted drugs in neuropathic pain and provides a new research direction for drug therapy of neuropathic pain.

KEY WORDS neuropathic pain transient Receptor Potential Vanilloid 1 inhibitor

neuropathic pain NPP Ė I Ϊ
I [1] Ƥ ϒ Ϊ ϒ Ψ Ϊ [3] ɟ ϒ Ϊ Ƥ ϒ
ϒ Ƥ ɔ ϐP ą Ă ’ ė
ϟ ϐɔ ~ ϟ ϐ ɲ ė Ă ϒ P [3] ɟ Ψ
~ ϐ Ҡ ϒ [2] ɟ Ϊ Ƥ Ϊ ϒ ɔ Ψ Ϊ ɟ

ΆΑ ΰ Na+ ΘCa2+ ΘK+ ی ١ ц
ی ɔ ١ ɔ ١ ɐ ɔ ɔ ١ ɐ
١ ɔ ١ ɣ [3] ɟ
ɔ ɮ Ң transient re
ceptor potential TRP Ά Ą
ę TRP Ψ TRPV1 transient receptor poten
tial vanilloid 1 ɟ ğĭ ی Ψ
ǫ̈ TRPV1 [4] ΄Y ğĭ Ψ
ה TRPV1 ; ţ̣ У [5] ɟ
Ά ΆΑ Ą
ɔ ɮ Ң Θ ΆΑ ę ΆΑ΄Ң ğĭ
Ψ ε
w[m] ~ ɟ

1

ɔ ɮ Ң transient receptor potential
TRP è ğĭ ŏ ל ١ ה
Ά ی Ψ ɔ ١ Ң א ל ١
Ό w ĭ΄ [6] ɟ TRP ŏ εv Y Жɟ
TRPC TRPV TRPM TRPP TRPML TRPA ١
TRPN [7] ɟ TRPC ΘTRPM ΘTRPA ١ TRPV Ж Ψ
ğĭ[m] 6 Y ת Ղ ΆΩ ҢНЬ ת
ε TRP TRP box ɟ TRP
TRP Θ [8] ɟ TRP
ẇ ж ١ Ǐ ' [9] ɟ TRP ל Ж
TRPC6 ɐ ה
΄ TRPA1 ɐ ң TRPM6 ɐ
TRPM1 [5] ɟ
TRPV1 transient receptor potential vanilloid 1
ẇ ɔ ١ [m] Ң
Нь ɔ ١ ɮ ɔ Ca2+
ę ђ Ϛ [m] ɟ
TRPV1 ' w Ǐ ΄Ң Ƀ
ьь ф ΘƧ ьь ١
΄Ң Ƀ ɟ
ɔ ١ ţ̣ ɐ ΘPH [e] ɟ ǫ̈
TRPV1 ' ΆΑ
φ[m] ţ̣ TRP Ca2+
Ǐ ˘ ɔ ה ♥
˚ Θ Ң [10] ~ Ψ
Ж ɟ TRPV1 ğĭ Ψ ١ ٨ م ج
ζ ğĭ ١ ɕ ẇ
ɔ [11 12] ɟ

2 TRPV1

ǫ̈ [m]
ε ɐ ر٥ ɐ
ɕ ɐ 5 ١˘ ɔ
Ő ך ΆΑ΄Ң [13] ɟ
ъ 1989 TRP ה w TRPV1
ל Ά Θ ΅Н
ɟ ; TRPV1 ΆΑ΄Ң Нь
ɟ
2.1 capsazepine
1994 [m] Y
S ΄Ң [14] ɟ S TRPV1 ɔ
΄ Ң
ɔ ɟ ğĭ Ψ
Θ ж ǫ̈ ę Нь í ζ
ğĭ w ; ΅Н Y Ẉ ɣ ε
ת Ѵ Ѵ ΆΑ΄ЦН ΄Ң / ж ی %

ų ̀Ω ۋ 5 ״ Ң ɔ
ɲ ך ų ų 2E 4Z N 3R 3 hydroxy 2 oxo 1 2 3 4 tetrahydro 5 quinolyl 5 4 isopropoxyphenyl 5 4 trifluoromethylphenyl 2 4 pentadienamide R 36b ̀Ω
ɻ ا Ǐ ɔ ´ ̈Ạ
Ca^{2+} Ə ΄Y w ̓Ḥ
ˬ ΄Y
ۋ سخ Ϗ ى
Ψ [18] ɻ
2.4 spinasterol
m Ḗ в ɔ ۱ Ϗ
ɔ Ə TRPV1 ̓Ḥ ̛ ς m
ɔ cyclooxygenase COX ̈Ạ ̓Ḥ ɻ ۋ
У ̈Ạ Ψ COX א У ۏ
̈Ω E2 PGE2 ' w Ə ε Ǐ
TRPV1 ɻ ۼ ״ c ̈Ạ COX ̈E
PGE2 У TRPV1 Ə ε
[19] ɻ
ۋ Ψ ı ̈E Ъ ~
̈E Ϗ Ψ [20] ɻ
ʗ ۋ ״ ϟ ا Ỹ ;
̈Ạ COX 1 ۱ COX 2 ɻ
m ΄Y ã TRPV1 ̓Ḥ ۱ COX
̈Ạ ̓Ḥ ۋ ~ ۱ ى Ψ Ḗ
Ə [20] ɻ
2.5 SZV 1287 3 4 5 diphenyl 1 3 oxazol 2 yl propanal oxime
SZV 1287 3 4 5 J نح 1 3 U 2 نح Γ 3 4 5 diphenyl 1 3 oxazol 2 yl propanal oxime m ى ɔ semicarbazide sensitive amine oxidase SSAO ̈Ạ ̓Ḥ ɻ SSAO ŭ ç نح Γ в ۱ ɔ [21] ' Ə Ъ TRPV1 ɔ ا ʃ φ ң ɻ ا Ǐ ۋ ȁ Ϗ ى Ψ SZV1287 ̈Ạ Ъ TRPV1 ɔ ɔ ɔ ɻ ۋ ى ۱ TRPV1 ۼ نح Ψ سخ ى ۋ SZV1287 7 ~ ╚ ң ۋ ۼ نح Ψ ʗ ɻ ɔ SZV1287 ״ c ̈Ạ SSAO ̈E У ̛ ς ' ̈Ạ TRPV1 Ə ʃ φ ε ى [22] ɻ

2.6 TRPV1 ŭ RNA
RNA small interfering RNA siRNA m ۋ 20 50 Y RNA RNA Ά ζ mRNA Ў ´ ʃ φ ̈Ạ ζ نح ۼ ɻ ۋ ى Ψ Ά ╥ ´ سخ ♥ Ϗ CCI Chronic constriction injury ṭ ۱ ṭ ج ╗ ɻ ה TRPV1 ۋ ۏ ع в ۱ هه ɻ Ǐ ~ TRPV1 siRNA ا ȁ ṭ ̈E ɻ ̛ Ъ Ψ ɱ ״ Extracellular signal regulated kinases ERK в ˬ CaM dependent kinases CaMKs ɻ Ẉ ۏ ERK ɔ ~ ۋ ẃ ' شح ۱ Ψ Ə CaMKs ל Ά ERK [4] ъ ל Ά У ɻ ۋ CCI ى Ψ CaMKII ɷERK ɔ Ə Ξ ج ╗ TRPV1siRNA ; TRPV1 ~ TRPV1 ۱ CaM KII ̈E ң ERK ɔ Ə ς ̈E TRPV1siRNA ч Ə ' Ά ; CaMKII ۱ ̈E ERK ɔ Ă [23] ɻ ה RNA short hairpin RNA shRNA m ה RNA ŭ ' RNA ̈Ạ نح ۼ ɻ Hirai [24] ~ TRPV1 AAV9 ا AAV9 shTRPV1 ~ Ϗ spared nerve injury SNI ى Ǐ AAV9 shTRPV1 ۋ ~ 10 28 50 ṭ Ӣ هه ẹ ђ Ξ ṭ Ξ ʗ ɻ ۋ 4 ۷ ~ AAV9 shTRPV1 DRG Ψ TRPV1 ң 55% ۋ Ψ ң 95% ɻ TRPV1 ۋ Ψ Ă Ə ς AAV9 sh TRPV1 Ə ۋ Ψ ״ ̀E Ə ɻ Ъ ~ TRPV1 siRNA ɷshRNA Ə ς ~ RNA long noncoding RNAs lncRNA ' w TRPV1 У Ə [25] ɻ Lnc RNAs RNA ´ II

`E У ѽ lnc RNA ‟
’ ğ Ǐ Ψ ה Ə ɟ
Lnc RNA BC168687 lnc RNAs ŏ φᵐ Ė I Ə
‟ ж Liu [25] ה ğ
Diabetic neuropathic pain DNP
DRG Ψ lnc RNA BC168687
ѫ ɟ Liu [26] ה lnc RNA
BC168687 siRNA DNP
ḭ e mechanical withdrawal thresholds
MWT ∤ ḭ ӣ thermal with
drawal latencies TWL Ą DRG Ψ
TRPV1 mRNA ˀ Ϛ ӈ DRG / 9ŒŠ ÞÐ DÂ — I —h Õ' …UÀ+±: zW !±W¡ !W¡ÄŒ V0 ™‘G† A

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ϊ Ή Ί Ω v Ψł ▌ 52.44% Ń ε ł ▌ 33.33% Ń Å ł 43 ϛ 84.31% Ń ε ł 43 ϛ 52.44% Ń

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