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BRIEF ARTICLE

Potentially predictive microRNAs of gastric cancer with metastasis to lymph node

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Abstract

AIM: To detect the expression of 60 microRNAs (miRNAs) in gastric cancer tissues and find new predictive biomarkers of gastric cancer with metastasis.

METHODS: The expressions of 60 candidate miRNAs in 30 gastric cancer tissues and paired normal tissues were detected by stem-loop real-time reverse transcription-polymerase chain reaction. After primary screening of miRNAs expression, 5 selected miRNAs were further testified in another 22 paired gastric tissues. Based on the expression level of miRNAs and the status of metastasis to lymph node (LN), receiver-operating-characteristic (ROC) curve were used to evaluate their ability in predicting the status of metastasis to LN.

RESULTS: Thirty-eight miRNAs expressions in gastric cancer tissues were significantly different from those in paired normal tissues ($P < 0.01$). Among them, 31 miRNAs were found to be up-expressed in cancer tissues and 1 miRNAs were down-expressed $\geqslant$ 1.5 fold *vs* paired normal gastric tissue. Five microRNAs (miR-125a-3p, miR-133b, miR-143, miR-195 and miR-212) were differently expressed between different metastatic groups in 30 gastric cancer biopsies ($P < 0.05$). Partial correlation analysis showed that hsa-mir-212 and hsa-mir-195 were correlated with the status of metastasis to LN in spite of age, gender, tumor location, tumor size, depth of invasion and cell differentiation. ROC analysis indicated that miR-212 and miR-195 have better sensitivities (84.6% and 69.2%, respectively) and specificities (both 100%) in distinguishing biopsies with metastasis to LN from biopsies without metastasis to LN.

CONCLUSION: miR-212 and miR-195 could be independent biomarkers in predicting the gastric cancer with metastasis to LN.

Key words: MicroRNA; miR-212; MiR-195; Gastric cancer; Metastasis to lymph node

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INTRODUCTION

Gastric cancer is the forth common malignancy and the second cause of death world widely[1]. Although radical gastrectomy with systemic lymph node (LN) dissection has saved many gastric cancer patients, the 5-year survivals are still far satisfactory[2]. Many evidences from large sample studies have shown that LN metastasis, the same to depth of invasion, histological differentiation, distant metastasis and tumor node metastasis stage, is one of the prognostic factors[3-6]. Currently we could get a little information of the status of LN metastasis before the operation while get most information from the histopathological diagnosis after the operation. Whether we could find a new way to predict LN metastasis became a new problem that faced us.

Accumulating evidences demonstrates that gastric cancer is a multigene-related disease with abnormal multistep developing progress of associated oncogenes and tumor suppressor, including various genetic and epigenetic alterations of oncogenes, tumor suppressor genes, DNA repair genes, cell cycle regulators and cell adhesion molecules take part in LN metastasis[7]. Thousands of genes have been reported involved in the process of gastric cancer, such as p53, muc1, cea, E-cadherin, p16 and CD44[8-11]. Large-scale molecular techniques as DNA microarrays have been widely utilized in investigation of the molecular complexity of gastric cancer and prognostic classification based on gene expression profile[12,13]. Recently, development of MicroRNAs (miRNAs) technique may complement and enhance our current understanding of the development and progression of gastric cancer and may evolute our way to predict the status of LN metastasis before the surgical operation.

miRNAs are an abundant class of endogenous noncoding RNAs (about 18~24 nt) that regulate the stability and expression efficiency of target mRNAs at the posttranscription level. By entirely or partially base-pairing to the 3'-untranslated region of target mRNAs, the miRNAs induce translation repression or degradation of the mRNAs[14], which plays a crucial role during various biological progresses, such as cell development, proliferation, differentiation and apoptosis[15]. Hypothetically, miRNAs are contributors to oncogenesis, functioning as tumor suppressors or oncogenes[16]. miRNAs can influence cancer development in many ways, such as the regulation of cell proliferation, cell transformation, cell death, and so forth. Recently studies have shown that some miRNAs were aberrantly expressed in many cancer tissues compared with paired normal tissues, such as the significant down-regulation of mir-143 and mir-145 in colon cancer[17] and up-regulation of mir-21 in breast cancer[18], thus underscoring the tremendous diagnostic and therapeutic potential of miRNAs in cancer. Furthermore, some miRNAs were closely associated with the prognosis of some specific cancers, for example, up-regulated mir-155 is linked to poor survival in pancreatic cancer[19]. A large-scale study of miRNAs in gastric cancer showed that two miRNAs (mir-143 and mir-145) were down-regulated[17,20] and one miRNA mir-27a correlated with LN metastasis[21], which implied that miRNAs were crucial markers for diagnosis and prognosis of cancer[22]. However, whether miRNA could predict the status of gastric cancer with metastasis to LN has not been identified.

In the present study, we first selected 60 miRNAs, which had been reported to participate in the regulation of cell growth, cell proliferation, cell differentiation, cell apoptosis, tumor cell invasion, migration in other cancers (The function of candidate miRNAs is shown in the appendix), as candidate, then, detected the expressions of 60 miRNAs in 30 paired gastric cancer tissues to select target miRNAs which were differently expressed in different status of metastasis to LN. The candidate miRNAs which expressions correlated with metastasis to LN were further testified in another 22 paired gastric tissues, and the correlationships between miRNAs expression and metastasis to LN were analyzed.

MATERIALS AND METHODS

Patients and biopsies

Paired specimens of gastric cancer tissues and corresponding normal gastric tissue (5 cm from cancer lesion without pathologically proven tumor cells), were obtained from patients with gastric cancer who underwent surgical resection at the First Affiliated Hospital of Wenzhou Medical College (Zhejiang Province, China) from December 2008 to April 2009. All the tissues were snap-frozen and stored in liquid nitrogen until total RNA was extracted. The histopathological diagnosis of gastric cancer was made by Department of Pathology, the First Affiliated Hospital of Wenzhou Medical College according to the criteria of the World Health Organization. All the patients did not received radiation therapy or chemotherapy before the surgical operation. Patients' characteristics of clinical-pathologic features were listed in Table 1.

Informed written consent was obtained from each patient and the study was approved by the Human Research Ethics Committee from the First Affiliated Hospital of Wenzhou Medical College.

RNA isolation

Total RNA was extracted from gastric cancer tissues and corresponding normal gastric tissues using Trizol Reagent (Invitrogen Life Technologies, United States) according to the manufacturer's instructions with some modifications. Briefly, the extracted RNAs re-suspended in isopropanol were incubated at -20 °C for at least 2 h (instead of 5 min at room temperature) to enhance precipitation efficiency of low-molecular-weight RNAs. Following a wash with 80% ethanol, RNA was re-suspended in diethylpyrocarbonate (DEPC)-treated water and stored at -80 °C. The concentration and purity of total RNA were qualified by the ultraviolet spectrophotometer at 260 nm and 280 nm. Only the RNA samples with ratio of $A_{260}/A_{280} > 1.8$ were used for the experiment.

Table 1 Clinical-pathological features of 30 biopsies

Clinicopathological variables	*n*
Gender	
Male	16
Female	14
Age	
< 60 yr	14
⩾ 60 yr	16
Tumor location	
Upper third	7
Middle third	16
Lower third	7
Tumor size	
< 5 cm	12
⩾ 5 cm	18
Histological type	
Well and moderately differentiated	11
Poorly differentiated	19
[1]Depth of invasion	
T1	4
T2	8
T3	18
Lymph node involvement	
N0	15
N1	8
N2	7
[1]Tumor node metastasis stage	
Stage Ⅰ	7
Stage Ⅱ	8
Stage Ⅲ	11
Stage Ⅳ	4

[1]According to the tumor node metastasis staging of Union for International Cancer Control.

Quantification of gastric specimen's miRNAs expression

Stem-loop real-time reverse transcriptase polymerase chain reaction (RT-PCR) was used according to Chen *et al*[23], Tang *et al*[24] and Xue *et al*[25], and miRNA hsa-mir-let7a as internal control in this study[26]. Briefly, 4 μg total RNA was reverse transcribed to synthesize cDNA. The 20 μL reverse transcription reaction system includes 4 μL RT Buffer (Toyobo), 0.5 μL RT ACE (Toyobo), 0.5 μL RNase inhibitor (Toyobo), 1 μL dNTP, 4 μg total RNA, 2 μL 1 μmol/μL stem-loop RT specific primer and RNase-free ddH_2O. Four internal controls including U6, let7a, hsa-mir-191 and hsa-mir-103 were reverse transcribed in parallel. The reaction condition was as follows: incubated at 16 ℃ for 30 min, 42 ℃ for 30 min, and 70 ℃ for 15 min finally. The synthesized cDNA was diluted up to 40 μL and preserved at -20 ℃ until use. The qRT-PCR reaction was performed on Applied Biosystems 7500 detection system by a 20 μL reaction system including 10 μL SYBR green real-time PCR Master Mix-plus (Toyobo, Japan), 2 μL Plus solution (Toyobo, Japan), each 2 μL specific Forward Primer and Reverse Primer, 1 μL RT product of total RNA and 3 μL DEPC water. All reactions were triplicate. The reaction was performed at 95 ℃ for 2 min, then followed by 40 amplification cycles of 95 ℃ for 15 s and 60 ℃ for 1 min. Melting curves were generated for each real-time RT-PCR to verify the specificity of each PCR reaction.

Data analysis

The Ct value (threshold cycle) is defined as the fractional cycle number at which the fluorescence passed the fixed threshold. Delta Ct (ΔCt) represent the expression difference between the target miRNA and the normalizer: $\Delta Ct = Ct_{mir} - Ct_{normalizer}$. Then delta delta Ct (ΔΔCt) was calculated using the equation: $\Delta\Delta Ct = \Delta Ct_{cancer\ tissue} - \Delta Ct_{normal\ tissue}$. The normalized miRNA in a sample is $2^{-\Delta\Delta Ct}$. For the matched normal tissue control sample ΔΔCt equal to zero and $2^{-\Delta\Delta Ct}$ equals to one. The expression levels of normalized miRNAs were characterized by their median and range (25th-75th percentile) because they did not fit the Gaussian distribution. Paired sample *t* test was used to evaluate the difference of miRNA expression between GC tissue and paired normal tissue and $P < 0.05$ was considered to have significant difference. Non-parameter tests were used to evaluate the differences of the miRNA expression between different groups: the Wilcoxon test for 2 paired groups (the tumor group and paired normal group) and the Mann-Whitney *U* test for the 2 independent groups. The partial correlation analysis was used to evaluate the relationship between some miRNA expression and the status of LN metastasis eliminating age, gender, tumor location, tumor size, invasion depth and cell differentiation. $P < 0.05$ was considered to be statistically significant. Receiver-operating-characteristic (ROC) curves was used to evaluate the sensitivity and specificity in predicting the LN metastasis based on the miRNA expression. The area under the ROC curve (AUC) and 95 percent confidence intervals were calculated. An AUC with a confidence interval that did not include the 0.5 value was considered that the miRNA had some ability to distinguish between the two groups. All calculations were performed with the software SPSS16.0.

RESULTS

Expression of 60 candidate miRNAs in gastric cancer specimens

The expressions of 60 candidate miRNAs were detected in 30 gastric cancer specimens by SYBR-green-based stem-loop real-time RT-PCR. As shown in Table 2, the expressions of the miRNAs in cancer tissues were very different from those of corresponding normal tissues. The relative expression of 38 miRNAs expressions ($2^{-\Delta\Delta Ct}$) in gastric cancer tissues were significantly different from those in paired normal tissues which set at 1.000 ($P < 0.01$), suggesting that those 38 miRNAs might be involved in the process of gastric tumorigenesis. Among them, 31 miRNAs were found to be up-expressed in cancer tissues and 1 miRNAs were down-expressed ⩾ 1.5 fold *vs* paired normal gastric tissue. Also, 5 miRNAs (hsa-mir-221, hsa-mir-15b, hsa-mir-181b, hsa-mir-199a-3p and hsa-mir-155) were in the highest expression levels, whereas hsa-mir-30b expression was the lowest.

Among the 30 candidate gastric cancer cases, 15 cases

Table 2 The relative expression of 60 candidate microRNAs ($2^{-\Delta\Delta Ct}$) in 30 gastric cancer specimens

MiRNA	Median	Percentile		[1]*P* value
		25%	75%	
Hsa-mir-106b	1.129	0.783	1.982	0.889
Hsa-mir-143	1.231	1.095	1.378	0.779
Hsa-mir-125a-5p	1.255	0.963	1.392	0.889
Hsa-mir-145	1.084	0.931	1.280	1.000
Hsa-mir-25	1.727	1.152	2.103	0.208
Hsa-mir-133b	1.127	0.938	1.314	0.779
Hsa-mir-195	0.989	0.754	1.534	0.889
Hsa-mir-374	1.005	0.800	1.599	0.779
Hsa-mir-451	0.594	0.442	1.636	1.000
Hsa-mir-1	1.228	0.950	2.135	0.327
Hsa-mir-141	0.973	0.663	1.125	0.208
Hsa-mir-200a	0.954	0.757	1.038	0.123
Hsa-mir-29c	0.867	0.664	1.042	0.123
Hsa-mir-29b	1.217	0.964	1.500	0.674
Hsa-mir-30b	0.600	0.542	0.782	0.017
Hsa-mir-26a	1.062	0.787	1.211	0.779
Hsa-mir-26b	1.257	0.838	1.369	0.779
Hsa-mir-144	1.548	1.251	2.118	0.123
Hsa-mir-103	2.103	1.259	2.339	0.050
Hsa-mir-h450b	1.500	1.061	2.601	0.208
Hsa-mir-191	1.770	1.007	2.216	0.161
Hsa-mir-200b	1.314	0.951	1.556	0.401
Hsa-mir-200c	1.151	1.101	1.545	0.161
Hsa-mir-203	1.790	1.464	2.498	0.069
Hsa-mir-429	1.944	1.250	2.028	0.050
Hsa-mir106a	1.279	1.139	1.917	0.069
Hsa-mir-15a	1.782	1.209	1.961	0.093
Hsa-mir-16a	1.145	1.112	1.338	0.017
Hsa-mir-17	1.603	1.396	1.921	0.017
Hsa-mir-155	2.663	1.873	3.557	0.012
Hsa-mir-18a	2.149	2.040	4.214	0.012
Hsa-mir-181b	2.535	2.195	2.635	0.012
Hsa-mir-421	2.141	1.518	2.498	0.012
Hsa-mir-92a	1.848	1.524	2.092	0.012
Hsa-mir-20a	1.596	1.037	2.071	0.036
Hsa-mir-125a-3p	1.729	1.191	2.997	0.036
Hsa-mir-199a-5p	1.645	1.157	2.624	0.069
Hsa-mir-93	2.583	1.250	3.139	0.025
Hsa-mir-222	1.373	1.309	2.488	0.025
Hsa-mir-15b	3.162	1.655	3.821	0.017
Hsa-mir-199a-3p	2.346	1.872	2.779	0.012
Hsa-mir-212	1.543	1.230	2.702	0.050
Hsa-mir-221	2.961	2.440	3.609	0.025
Hsa-mir-147	2.162	1.928	6.019	0.012
Hsa-mir-205	2.008	1.727	15.946	0.017
Hsa-mir-30d	1.614	1.346	2.17	0.017
Hsa-mir-363	1.732	1.612	1.928	0.012
Hsa-mir-23b	1.744	1.339	2.116	0.017
Hsa-mir-214	1.768	1.69	1.902	0.012
Hsa-mir-497	1.520	1.204	2.328	0.017
Hsa-mir-let7c	1.759	1.276	2.300	0.012
Hsa-mir-99a	1.286	1.220	2.734	0.012
Hsa-mir-193b	1.616	1.387	2.554	0.012
Hsa-mir-31	1.749	1.355	3.234	0.012
Hsa-mir-let7b	1.287	1.155	2.071	0.017
Hsa-mir-487b	1.598	1.424	2.855	0.017
Hsa-mir-h450a	1.435	1.116	1.609	0.123
Hsa-mir-18b	1.691	1.413	3.164	0.069
Hsa-mir-19b	1.411	1.248	1.726	0.093
Hsa-mir-19a	1.687	1.209	1.823	0.093
Hsa-mir-let7e	1.195	1.061	1.459	0.123

The relative expression of miRNA ($2^{-\Delta\Delta Ct}$) in tumor samples, with that in nontumor control samples set at 1.000. [1]*P*: The Mann-Whitney *U* test for the different expression of microRNA in different group.

Table 3 Five miRNAs expression in different lymph node metastasis groups

MiRNA	LN Negative (n = 15)	LN Positve (n = 15)	[1]*P* value
miR-125a-3p	1.87 (1.27, 2.32)	0.81 (0.49, 1.15)	0.02
miR-133b	1.31 (1.08, 1.59)	0.74 (0.41, 0.97)	0.04
miR-143	1.38 (1.23, 1.57)	0.57 (0.16, 1.03)	0.04
miR-195	1.53 (1.18, 2.52)	0.46 (0.31, 0.64)	0.02
miR-212	2.70 (2.14, 3.16)	1.06 (0.93, 1.18)	0.02

[1]*P*: The Mann-Whitney *U* test for the different expression of microRNA in different groups. LN: Lymph node.

Table 4 Partial correlation analysis of 5 miRNAs expressions and lymph node metastasis

MicroRNA	Correlation coefficient	*P* value
miR-125a-3p	-0.451	0.091
miR-133b	-0.014	0.961
miR-143	-0.25	0.369
miR-195	-0.57	0.026
miR-212	-0.616	0.014

associated with LN metastasis, whereas 15 did not. Using the Mann-Whitney U test, we found that 5 miRNAs (hsa-mir-125a-3p, hsa-mir-133b, hsa-mir-143, hsa-mir-195 and hsa-mir-212) in gastric cancer patients with LN metastasis were quite different from those in patients without LN metastasis (Table 3). hsa-mir-125a-3p and hsa-mir-212 in patients with LN metastasis were lower than those in patients without LN metastasis while hsa-mir-143 and hsa-mir-195 were higher than those in patients without LN metastasis. But the expressions of the miRNAs did not correlate with age, gender, tumor location, tumor size and depth of invasion (data not shown).

Correlation between the miRNAs expressions and lymph node metastasis of gastric cancer

As the expressions of hsa-mir-125a-3p and hsa-mir-212 in patients with LN metastasis were lower than those in patients without LN metastasis while hsa-mir-143 and hsa-mir-195 were higher than those in patients without LN metastasis, partial correlation analysis for eliminating age, gender, tumor location, tumor size, invasion depth and cell differentiation showed that hsa-mir-212 and hsa-mir-195 were correlated with LN metastasis in spite of the status of cell differentiation (Table 4).

Predicting value based on miRNAs expression in lymph node metastasis

Five candidate miRNAs which correlated with metastasis to LN were selected and re-examined in another 22 gastric cancer biopsies to evaluate the predicting value in metastasis to LN (Figure 1). ROC analysis indicated hsa-mir-212 yielded an AUC of 0.915 (95% CI: 0.790-1.039). At the cutoff value of 1.439, hsa-mir-212 had 84.6% sensitivity and 100% specificity in discriminating gastric cancer biopsies with metastasis to LN. Whereas, hsa-mir-195 yielded AUC of 0.821 (95% CI: 0.634-1.007) with 69.2%

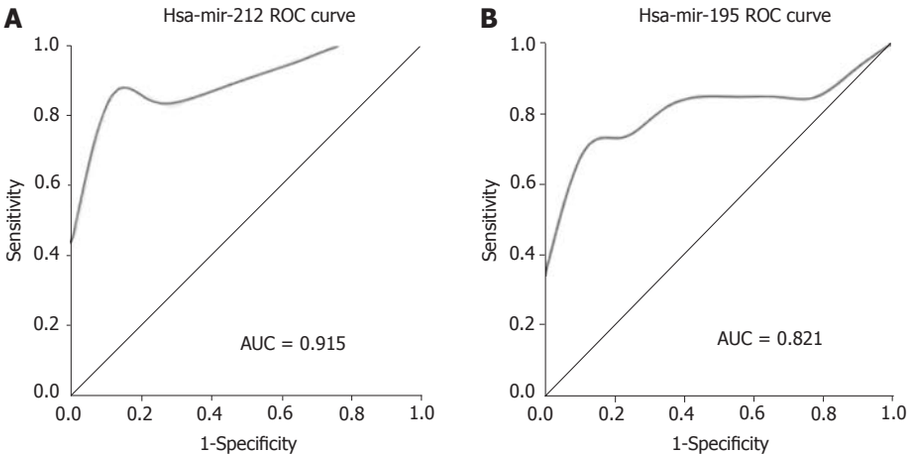

Figure 1 Receiver operating characteristics curve analysis using hsa-mir-212 and hsa-mir-195 for discriminating gastric cancer biopsies with or without metastasis to lymph node. A: Hsa-mir-212 yielded an AUC (the areas under the receiver operating characteristics curve) of 0.915 (95% CI: 0.790-1.039) with 84.6% sensitivity and 100% specificity in discriminating gastric cancer biopsies with metastasis to lymph node (LN); B: Hsa-mir-195 yielded AUC of 0.821 (95% CI: 0.634-1.007) with 69.2% sensitivity and 100% specificity of in discriminating gastric cancer biopsies with metastasis to LN.

sensitivity and 100% specificity of in discriminating gastric cancer biopsies with metastasis to LN.

DISCUSSION

Recently, many researches have demonstrated that miRNAs played an important role as either an oncogene or tumor suppressor gene in the initiation and progression. Though a few studies on miRNAs expression of gastric cancer have been carried out, and aberrant expressions in gastric cancer have been identified. However, few reports had screened the miRNAs expression specifically associated with LN metastasis, which was a prognostic factors to gastric cancer patients. In this study, firstly the expressions of 60 candidate miRNAs were detected in 30 gastric cancer specimens by SYBR-green-based stem-loop real-time RT-PCR, and 38 of 60 miRNAs expressions in gastric cancer tissues were found to be significantly different from those in paired normal tissues ($P < 0.01$). Among them, 31 miRNAs were found to be up-expressed in cancer tissues and 1 miRNA were down-expressed $\geqslant$ 1.5 folds *vs* paired normal gastric tissue, suggesting that abnormal expression of those miRNAs may play a role in the development of gastric tumorigenesis.

The abnormal expressions of some miRNAs had been reported in several cancers, for example, hsa-mir-155 was over-expressed in pancreatic tumor[27], thyroid tumor[28], cervical cancer[29] and the up-regulated expression of hsa-mir-155 was related to a poor prognosis of patients with pancreatic cancer[19]. hsa-mir-15b was up-regulated in pancreatic cancer[30], colorectal cancer[31] and cervical cancer[29]. The highly expressed hsa-mir-221, one member of mir-221/222 cluster, was up-regulated in glioblastoma[32], bladder cancer[33]. Three reports demonstrated that mir-199a was down-regulated in bladder tumor[34], ovarian cancer[35] while up-regulated in hepatoblastoma[36]. hsa-miR-143 and hsa-miR-145 were down-regulated in colon cancer[37] and nasopharyngeal cancer[38] and gastric cancer[17]. hsa-mir-143 and hsa-mir-145 have been identified to have a suppressive effect on cell growth and the reduction in the level of mir-143 and mir-145 positively contributed to the proliferation in gastric cancer cell[17]. hsa-mir-212 was downregulated and repressed growth by targeting methyl-CpG-binding protein MeCP2 in gastric cancer cell line[39]. Therefore, the abnormal expression of these miRNAs may be correlated to the development cancers.

Recently, miR-373 and miR-520c have been reported to be as metastasis-promoting miRNAs that promote tumor invasion and metastasis, whereas miR-335, miR-206, and miR-126 have been as suppressors of breast cancer metastasis[40,41]. The down-regulation of has-mir-195 has been observed in primary peritoneal carcinoma[42] and bladder tumor[34]. Introduction of miR-195 dramatically suppressed the ability of hepatocellular carcinoma and colorectal carcinoma cells to form colonies *in vitro* and to develop tumors in nude mice[43]. However, our data showed that hsa-mir-195 and hsa-mir-212 were down-regulated in gastric cancer with LN metastasis in spite of the status of tumor cell differentiation.

Li *et al*[44] recently reported that seven microRNAs (miR-10b, miR-21, miR-223, miR-338, let-7a, miR-30a-5p, miR-126) as a risk signature was an independent predictor of overall survival and relapse-free survival. Here we reported that the down-regulation of hsa-mir-212 and hsa-mir-195 were not only associated with lymph metastasis for the first time but also had better predicting value in LN metastasis.

Taken together, abnormal expression of miRNAs may be correlated with the development and progression of gastric cancer, the down-regulation of hsa-mir-212 and hsa-mir-195 were correlated with LN metastasis and couuld distinguish patients with LN metastasis from patients without LN metastasis. Further works and large samples of gastric cancer are needed to validate the diagnostic criteria of miRNA for gastric cancer with LN metastasis and identify target mRNAs from candidate.

COMMENTS

Background

Gastric cancer is one common solid tumor world widely. Almost one million people die from it every year. Although patients received radical gastrectomy with systemic lymph node (LN) dissection the 5-year survival is still far satisfactory. Gastric cancer with metastasis to LN is one important prognostic factor. As surgeons could get little information of metastasis to LN before the operation some patients who should receive radical gastrectomy received operation style of endiscopic mucosal reseceion or laparoscopy-assisted gastrectomy. So patients

could benefit from the evaluation of metastasis to LN before surgical operation.

Research frontiers

Accumulating evidence indicate that gastric cancer metastasized to LN is the results of various genetic and epigenetic alternations of oncogens, tumor supressor genes, DNA repair genes, cell cycle regulators and cell adhension molecules. Hundreds of genes have been reported involved in the process of metastasis and this made the study of metastasis a more complex problem. Recently researches have focused their study on the aberrantly expressed microRNA in gastric caner. However, there haven't been a report about the preditive value in evaluating the status of gastric cancer metastasized to LN basing on the expression level of microRNA.

Innovations and breakthroughs

Recent reports have demonstrated many microRNAs were upregulated or downregulated in gastric cancer. This is the first study to report that hsa-mir-212 and hsa-mir-195 had better sensitivity and specificity in distinguishing gastric cancer biopsies with metastasis to LN from gastric cancer biopsies without metastasis to LN.

Applications

By understanding the predictive value of microRNA in evaluating the status of gastric cancer metastasized to LN, this study approached the problem to identify a diagnostic criteria for gastric cancer biopsies with metastasis to LN employing miRNA as biomarkers and help surgeons to evaluate the status of metastasis to LN before surgical operation and choose reasonable operation style for patients.

Terminology

microRNAs are an abundant class of endogenous non-coding RNAs that regulate the stability and expression efficiency of target mRNAs at the post-transcription level. Almost 50% microRNAs located at or near to the fragile site of tumor-associated genes. MicroRNAs which were near to the gene promoting metastasis of gastric cancer should be aberrantly expressed. This signature make it feasible that microRNA could distinguish gastric cancer biopsies with metastasis to LN from gastric cancer biopsies without metastasis to LN.

Peer review

This is a very interesting study in which the investigators approached the problem to identify a diagnostic criteria for gastric cancer biopsies with LN metastasis employing miRNA as biomarkers.

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