Comparison of nuclear matrix proteins between gastric cancer and normal gastric tissue

Qin-Xian Zhang, Yi Ding, Zhuo Li, Xiao-Ping Le, Wei Zhang, Ling Sun, Hui-Rong Shi

Abstract
AIM: To study the alteration of nuclear matrix proteins (NMPs) in gastric cancer.

METHODS: The NMPs extracted from 22 cases of gastric cancer and normal gastric tissues were investigated by SDS-PAGE technique and the data were analyzed using Genetools analysis software.

RESULTS: Compared with normal gastric tissue, the expression of 30 ku and 28 ku NMPs in gastric cancer decreased significantly (P<0.002, =0.001, P<0.05). No significant difference was found in the expression of the two NMPs between the various differentiated grades (P=0.947, P=0.356) and clinical stages of gastric cancer (P=0.920, P=0.243, P>0.05).

CONCLUSION: The results suggested that the alteration of NMPs in gastric cancer occurred at the early stage of gastric cancer development.

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Statistic analysis
Data were analyzed using nonparametric statistics with SPSS 10.0 statistic software and P<0.05 was considered statistically significant.

RESULTS
On the gel stained with Coomassic brilliant blue R-250, many bands were exhibited in both gastric cancer and normal gastric tissue, which suggested that NMPs were abundant in these tissues. The bands of 30 ku and 28 ku NMPs in the gastric cancer were stained more lightly than those in the normal gastric tissue (Figure 1). Analyzed with Genetools quantitative software, the expression of 30 ku and 28 ku NMPs in normal gastric tissues was significantly higher than those in gastric cancer (P<0.05). The difference of the expression of 30 ku and 28 ku NMPs between well and moderately differentiated and...
poorly differentiated gastric cancers was not significant \( (P<0.05) \). There was no significant difference in the expression of the two NMPs between stage I, II and stage III, IV \( (P>0.05) \) (Table 1).

**Figure 1** SDS-PAGE of nuclear matrix 1 gastric carcinomatous tissue; 2 adjacent cancer tissue; 3 normal tissue; 4 marker.

**Table 1** Comparison of the 30 ku, 28 ku bands between gastric cancer tissues and normal tissues

| Group                  | 30 ku | 28 ku |
|------------------------|-------|-------|
|                        | \( n \) | \( T \) | \( Z \) | \( T \) | \( Z \) |
| Normal tissue group*   | 22    | 7.25  | -3.165 | 4.33  | -3.263 |
| Gastric cancer group   | 22    | 12.44 | 14.19  |       |       |
| Well and moderately    | 10    | 11.60 | -0.066 | 12.90 | -0.923 |
| differently differentiated |     |       |       |       |       |
| Poorly differentiated  | 12    | 11.42 | 10.33  |       |       |
| Stage I, II            | 9     | 11.33 | -1.00  | 13.44 | -1.169 |
| Stage III, IV         | 13    | 11.62 | 10.15  |       |       |

\( T \): mean of rank sum, \( Z \): z value \( P<0.05 \) vs gastric cancer.

**DISCUSSION**

NM is the structural framework of the nucleus[7], and is involved in a variety of cell functions, including DNA replication[9], RNA transcription[9], architecture of chromatin[9], carcinogenesis[11] and apoptosis[9]. The study on the relationship between NMPs and carcinogenesis has been carried out for a few years. In the experiment of Spencer et al.[9], specific changes in NMPs of breast cell line were identified by two-dimensional gel electrophoresis. NMP66 was evaluated as a potential biomarker for early breast cancer in large-scale clinical trials[9,11]. The extent of chromosomal rearrangements correlates positively with the level of expression of the nuclear matrix high mobility group (HMG) proteins HMG I(Y) when tested in three human prostate cancer cell lines (PC-3, DU145, LNCaP)[9]. Using both one-dimensional and high-resolution two-dimensional immunoblot analyses, Leman et al.[9] found that, in the transgenic adenocarcinoma of mouse prostate (TRAMP) model, HMG I(Y) was an NMP expressed as two protein bands with a molecular mass of 22-24 ku and HMG I(Y) expression was correlated with neoplastic and malignant properties in late stage of prostate tumor TRAMP model. In 26 pairs of human prostate cancer and normal tissue, Ishiguro et al.[9] identified a specific upregulated gene encoding a 55 ku nuclear matrix protein (nmt55) by RT-PCR and real time quantitative PCR, nmt55 gene expression in human prostate cancer tissue was higher (20/26) than that in normal prostate tissue.

NMP22 has been identified as a tumor marker for transitional cell carcinoma of urinary tract[27] and bladder cancer[20-21]. Eissa et al.[20] evaluated the diagnostic efficacy of NMP22, fibronectin and urinary bladder cancer antigen (UBC) in comparison with voided urine cytology on the detection of bladder cancer. They found that NMP22 and fibronectin had superior sensitivities compared to UBC and voided urine cytology, while NMP22 and voided urine cytology had the highest specificities. Xu[23] reported that the examination of NMP22 in urine was a rapid and effective way to detect the recurrence of bladder cancer. The urinary NMP22 levels were significantly higher in the renal cell carcinoma group than in the control group. The urinary NMP22 might be used in the evaluation of patients at risk of renal cell carcinoma[24]. Konety et al.[25] reported that the BLCA-4 was a very sensitive and specific marker for bladder cancer.

NMPs alterations were also associated with the cancer of digestive tract. Chen et al.[26] found that the interaction between HPV-16 E6 and nuclear matrix might contribute to virus induced carcinogenesis in esophageal carcinoma. Brunagel et al.[27] analyzed the NMPs expression by high-resolution two-dimensional gel electrophoresis, and found that the NMP composition was able to differentiate liver metastases from normal liver tissue and normal hepatocytes. In 2003, they identified an NMP, calreticulin, which was expressed much more strongly in colon cancer compared to adjacent and normal colon tissue[25]. In our study, we found that the expression of 30 ku, 28 ku NMPs was significantly reduced in gastric cancer when compared with that in the normal gastric tissue \( (P<0.05) \). There were no significant differences in the expression of these two proteins between the various differentiation grades and clinical stages of the gastric cancer. The results suggested that the changes of NMPs in gastric cancer might occur at early stage of the tumor development.

Matrix attachment regions (MARs) are postulated to anchor chromatin onto the NM, thereby organizing genomic DNA into topologically distinct loop domains that are important in replication and transcription[29]. The p300-SAF-A interactions at MAR elements of nontranscribed genes might poise these genes for transcription[30]. NM was a key locus for CK2 signaling in the nucleus[31]. Expression of p16 gene was significantly reduced in gastric cancer. The down-regulated expression of 30 ku, 28 ku NMPs in gastric cancer might be related to the down-regulated expression of p16 gene. In our previous study, we found the hypermethylation, mutation and microsatellite instability of p16 gene in gastric cancer. The binding of NMPs to the upstream of p16 gene and its relation to the down regulated expression of p16 gene in gastric cancer will be studied further.

**REFERENCES**

1. Leman ES, Getzenberg RH. Nuclear matrix proteins as biomarkers in prostate cancer. J Cell Biochem. 2002; 86: 213-223
2. Holaska JM, Wilson KL, Mansharamani M. The nuclear envelope, lamins and nuclear assembly. Curr Opin Cell Biol 2002; 14: 357-364
3. Pavao M, Huang YH, Hafer LJ, Moreland RB, Traish AM. Immunodetection of nmt55/p54nrb isoforms in human breast cancer. BMC Cancer 2001; 1: 15
4. Ishii T, Okadome A, Takeuchi F, Hiratsuka Y. Urinary levels of nuclear matrix protein 22 in patients with urinary diversion. Urology 2001; 58: 940-942
5. Brungel G, Vietmeier BN, Bauer AJ, Schoen RE, Gerzenberg RH. Identification of nuclear matrix protein alterations associated with human colon cancer. Cancer Res 2002; 62: 2437-2442
6. Leman ES, Arlotti JA, Dhir R, Greenberg N, Getzenberg RH. Characterization of the nuclear matrix proteins in a transgenic mouse model for prostate cancer. J Cell Biochem 2002; 86: 203-212
7. Philimonenko VV, Fischon JE, Hozak P. The nucleoskeleton: a permanent structure of cell nuclei regardless of their transcriptional activity. Exp Cell Res 2001; 264: 201-210
8. Djeliova V, Russev G, Anachkova B. Dynamics of association of origins of DNA replication with the nuclear matrix during the cell cycle. Nucleic Acids Res 2001; 29: 3181-3187
9. Blencowe BJ, Faivre S, Issner R, Nickerson JA,
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