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• *BRIEF REPORTS* •

Raman spectra of single cell from gastrointestinal cancer patients

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Abstract

AIM: To explore the difference between cancer cells and normal cells, we investigated the Raman spectra of single cells from gastrointestinal cancer patients.

METHODS: All samples were obtained from 30 diagnosed as gastrointestinal cancer patients. The flesh tumor specimen is located in the center of tumor tissue, while the normal ones were 5 cm away from the outside tumor section. The imprint was put under the microscope and a single cell was chosen for Raman measurement. All spectra were collected at confocal Raman micro-spectroscopy (British Renishaw) with NIR 780 nm laser.

RESULTS: We measured the Raman spectra of several cells from gastrointestinal cancer patients. The result shows that there exists the strong line at 1 002 /cm with less half-width assigned to the phenylalanine in several cells. The Raman lines of white cell were lower and less, while those of red cell were not only higher in intensity and more abundant, but also had a particular C-N breathing stretching band of pyrrole ring at 1 620-1 540 /cm. The line at 1 084 /cm assigned to phosphate backbone of DNA became obviously weaker in cancer cell. The Raman spectra of stomach cancer cells were similar to those of normal cells, but the Raman intensity of cancer cells was much lower than that of normal cells, and even some lines disappear. The lines of enteric cancer cells became weaker than spectra above and many lines disappeared, and the cancer cells in different position had different fluorescence intensity.

CONCLUSION: The Raman spectra of several cells from cancer patients show that the structural changes of cancer cells happen and many bonds rupture so that the biological function of cells are lost. The results indicate that Raman spectra can offer the experiment basis for the cancer diagnosis and treatment.

Key words: Raman spectra; Gastrointestinal cancer

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INTRODUCTION

Cancer is one of the most serious diseases threatening human health and life, and the influence of this disease becomes increasing. Due to the pathogeny of cancer and some correlative illness have not been found, and the effective diagnosis and complete therapy cannot be carried out at present. It is impossible to control the progress of the state of the illness for cancer patient in terminal stages. Therefore, early diagnosis and timely therapy is the most effective approach in improving the surviving chance of patient. It is very difficult to diagnose cancer in modality because the early symptom of cancer is not evident and it has no distinct difference from that of some other illness. Therefore, it is a research emphasis to find new, effective diagnosis technology and treatment method.

The vibration spectrum has promising potential as an analytical tool for diagnosing cancer because it can probe the chemical composition and molecular structure of the normal and pathological tissue, so that researchers have paid much attention to the field over the past decade[1-5]. The Raman method has the relative lower requirement to the preparation of sample, ordinary biological sample such as cell, living tissue, DNA and RNA can be measured directly. The measurement has no damage to sample and a large number of data can easily be obtained. Therefore, many application of Raman spectrum have been gained in biology, medicine, medicament analysis and filtration[6-10]. But to date, there is some lack of knowledge about the Raman spectra of a single cancer cell in the former reports. In the present paper, we report a study about the Raman spectra of single cells of stomach, rectal, and colon cancer tissue and corresponding normal cells.

MATERIALS AND METHODS

All samples were collected from the imprint with desquamation cells from fresh sample after operating on 30 diagnosed patients of Liaocheng People's Hospital (20 men and 10 women, of ages 30-70 years). The tumor specimens were

taken from the part of cancer tissue, the normal samples were 5 cm away from the outside cancer tissue. The residual samples after the patches were marked were stained and sliced so as to be analyzed and diagnosed in pathology.

All spectra were collected at confocal Raman micro-spectroscopy (British Renishaw), with NIR 780 nm laser whose power was maintained at 25 mW and the spectral resolution was less than 2 /cm.

RESULTS

The Raman spectra of single red cell and a string of red cell are shown in Figure 1A. The red cell is mainly composed of membrane and cytoplasm which has a large number of hemoglobin. We can see that hemoglobin has a typical band at 1 620-1 540 /cm in Figure 1A, which is assigned to C-N breathing stretching band of pyrrole ring. This band cannot be measured in other cells. There exists the peak at 1 654 /cm assigned to α-helix, which has low intensity, but the peaks assigned to β-folding and random coil are not found. The band of amide-III at 1 246 /cm is wide and strong, which is assigned to the overlapping of α-helix, β-folding and random coil. The Raman lines at 1 447, 1 369 and 1 340 /cm correspond to the deformation vibration of CH_2 and CH_3. The strong line with 4 /cm half-width at 1 001 /cm assigned to the phenylalanine is very steady and can be used as a standard line with respect to other Raman lines. The frequencies of other Raman lines and their assignment are shown in Table 1.

The Raman spectra of single white cell are shown in Figure 1B. Its peaks are very weak except the band of phenylalanine at 1 003 /cm.

The Raman spectra of lymphocyte are shown in Figure 1C. We can see the wide and strong band at 1 658 /cm, which is assigned to the characteristic vibration of Amide-I and may be correlated to the overlapping of α-helix, β-sheet and random coil. The strong Raman lines at 1 447 /cm corresponds to the deformation of CH_2 and CH_3. The assignment of other Raman lines is shown in Table 1.

The Raman spectra of normal cell from rectal cancer patient are shown in Figure 2A similar to that of the lymphocyte. Figures 2B and 2C show the Raman spectra of cancer cells on rectal smooth muscle and rectal, respectively. The Raman line assigned to phenylalanine is still distinct and its intensity becomes low in cancer cells. There exist the Raman lines of Amide-I, CH_2 and CH_3 in two cases, these lines become weak and other lines disappear. The cancer cells in different position have distinctly different fluorescence intensity. The Raman spectra of colon cancer cells in Figure 3A are similar to that of rectal cancer cells in Figure 2C.

The Raman spectra of stomach cancer cells are shown in Figure 3B. Its Raman spectra are similar to the normal cells, but the Raman intensity is much lower than that of normal cells. The peak at 1 084 /cm of phosphate backbone of DNA disappears.

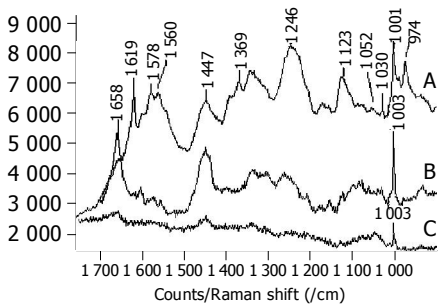

Figure 1 Raman spectra of several cells from cancer patients. A: red cell; B: lymphocyte; C: white cell.

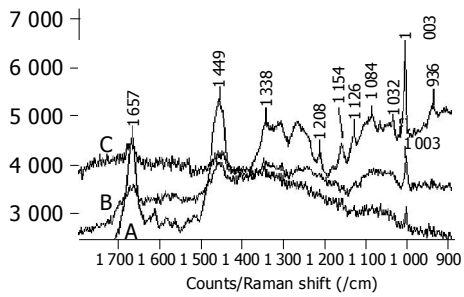

Figure 2 Raman spectra of normal and cancer cell from rectum cancer patients. A: normal cell; B: cancer cell on rectal smooth muscle; C: rectal cancer cell.

Table1 Peak position and assignments of Raman spectra of several cells from cancer patients

Red cell	White cell	Lymphocyte	Normal cell	Colon, rectal cancer cell	Stomach cancer cell	Assignments
1 654	1 658	1 658	1 657	1 662	1 660	Amide-I , α-helix
1 619						Tyr, Trp v (C = C)
1 578						Phe v (C = C) symmetric
1 560						Trp
1 548						Trp
1 447	1 445	1 447	1 449	1 449	1 449	$\delta(CH_2, CH_3)$
1 369						δCH_2
1 340		1 338	1 338		1 342	δCH_2
1 246		1 247	1 247		1 248	Amide-III
		1 209	1 208		1 206	Tyr, Phe
1 123		1 126	1 126		1 126	v (C-N)
		1 084	1 084			v (C-N)
1 052		1 053	1 054		1 054	v (C-N)
1 030		1 032	1 032		1 032	Phe v (C-H)
1 001	1 003	1 003	1 003	1 002	1 002	Phe v (C-C) symmetric
Symmetric						
974						CH_2
936		937	936		938	v (CC)skeletal α-helix

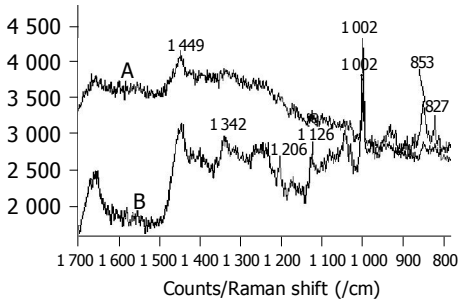

Figure 3 Raman spectra of cancer cell. A: colon cancer cell; B: stomach cancer cell

DISCUSSION

We studied the Raman spectra of several cells from gastrointestinal cancer patients. There exists the strong line at 1 002 /cm with less half-width assigned to the phenylalanine in several cells, whose intensity is not easy to change and can often be a standard of Raman lines of cell. The Raman intensity of white cell is low and lacking, while that of red cell is high and abundant and it has a particular C-N breathing stretching band of pyrrole ring from 1 620 to 1 540 /cm. The relative intensity of 1 084 /cm of phosphate backbone of DNA becomes obviously weak in cancer cells. The Raman spectra of stomach cancer cells are similar to the normal cells, but the Raman intensity is much lower than that of normal cells. The lines of enteric cancer cells become weaker than that of stomach cancer and many lines disappear and the cancer cells in different part have different fluorescence intensity. These conclusions show that the structure changes of cancer cells happen and many bonds rupture so that the biological function of cells are lost. The results indicate that Raman spectra may offer the experiment basis for cancer diagnosis and treatment.

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