



## Relationship between loss of heterozygosity of *deleted in colorectal carcinoma* gene microsatellites and prognosis of colorectal adenocarcinoma

Po Zhao, Ying-Chuan Yu, De-Wen Wang, Zhi-Ping Wang, Xin-Zhao Xu, Ping-Yong Yi, Ya-Bing Gao, Guang-Hua Yang

Po Zhao, Department of Pathology, Chinese PLA General Hospital, Beijing 100853, China

Ying-Chuan Yu, Ping-Yong Yi, Guang-Hua Yang, Department of Pathology, West China University of Medical Sciences, Chengdu 610041, Sichuan Province, China

De-Wen Wang, Zhi-Ping Wang, Ya-Bing Gao, Department of Pathology, Academy of Military Medical Sciences, Beijing 100850, China

Xin-Zhao Xu, Department of Pathology, General Hospital of Chinese PLA, Jinan Command Area

Po Zhao, MD and PhD, Associate Professor of Pathology, Head of Molecular Pathology Lab, has published 40 papers.

Author contributions: All authors contributed equally to the work.

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Correspondence to: Dr. Po Zhao, MD, PhD, Associate Professor, Department of Pathology, Chinese PLA General Hospital, Beijing 100853, China  
Telephone: +86-10-66887329-6253

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### Abstract

**AIM:** To investigate the relationship between the loss of heterozygosity (LOH) of microsatellites on the *deleted in colorectal carcinoma* (*DCC*) gene and prognosis of colorectal adenocarcinoma.

**METHODS:** A retrospective study of 58 colorectal adenocarcinoma cases with follow-up data and paired control normal mucosal tissues from 1983 to 1985 from files from the West China University of Medical Sciences Department of Pathology was carried out by PCR microsatellite analysis. Sixteen, 35, and seven cases had well-, moderately, and poorly differentiated tumors, respectively; 11, 30, and 17 cases were staged as Dukes' A, B, and C, respectively.

**RESULTS:** LOH of *DCC* microsatellites was detected in 18 cases

(31.0%). The 5-year survival rate between LOH-positive and LOH-negative patients was 44.4% and 77.5%, respectively ( $P < 0.05$ ). The results suggest that LOH of *DCC* microsatellites correlate with prognosis but not with differentiation ( $P > 0.05$ ) and Dukes' stage ( $P > 0.05$ ) in colorectal adenocarcinoma.

**CONCLUSION:** LOH of *DCC* microsatellites may be a marker of malignancy. Combined with the traditional prognostic indicators, LOH can predict prognosis of colorectal adenocarcinoma.

**Key words:** Colorectal neoplasms; Polymerase chain reaction (PCR); Oncogenes; Adenocarcinoma; Heterozygote; Prognosis

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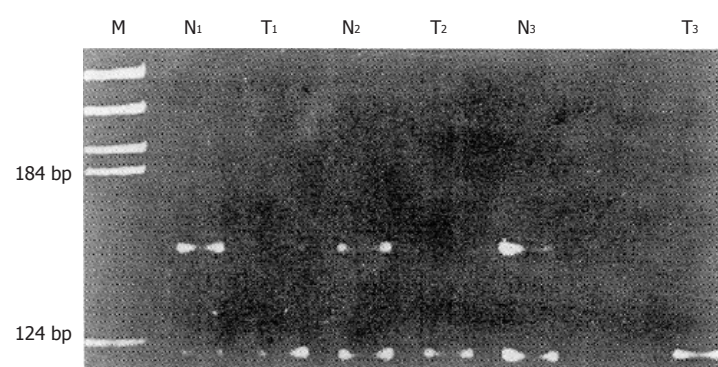
Zhao P, Hu YC, Wang DW, Wang ZP, Xu XZ, Yi PY, Gao YB, Yang GH. Relationship between loss of heterozygosity of *deleted in colorectal carcinoma* gene microsatellites and prognosis of colorectal adenocarcinoma. *World J Gastroenterol* 1997; 3(2): 121-122 Available from: URL: <http://www.wjgnet.com/1007-9327/full/v3/i2/121.htm> DOI: <http://dx.doi.org/10.3748/wjg.v3.i2.121>

### INTRODUCTION

The *deleted in colorectal carcinoma* (*DCC*) gene is located on chromosome 18q21. In colorectal adenocarcinoma, there is an allelic deletion on the *DCC* gene and its level of expression is decreased, but few studies on the relationship between loss on the *DCC* gene and the prognosis of colorectal adenocarcinoma have been published to date. We used a PCR microsatellite method with a pair of primers flanking a dinucleotide microsatellite located within a *DCC* gene intron to study the relationship between the loss of heterozygosity (LOH) of *DCC* gene microsatellites and the prognosis of colorectal adenocarcinoma.

### MATERIALS AND METHODS

Paraffin blocks containing normal and neoplastic tissues from 71 patients with adenocarcinoma of the colon and rectum were selected for the study from files in the West China University of Medical Sciences Department of Pathology. The hematoxylin and eosin (H and E) slides from these patients were examined. Tumors were graded as well, moderately, or poorly differentiated and were assigned to Dukes' stage A, B, or C based on the standard criteria. All patients had a 5-year follow up after surgery. The PCR microsatellite method was performed as described previously<sup>[1,2]</sup> but with slight modifications, i.e., ethidium bromide instead of isotope staining.



**Figure 1** Loss of heterozygosity of *deleted in colorectal carcinoma* gene microsatellites in colorectal adenocarcinoma. M: PBR322 Hae III molecular marker; N: paired normal tissues; T: tumor tissues; T<sub>2</sub>, T<sub>3</sub>: Loss of heterozygosity of *deleted in colorectal carcinoma* gene microsatellites.

## RESULTS

### Frequency of LOH

Fifty-eight amplified cases were informative for the marker of heterozygosity; 18 cases (31.0%) showed LOH. Figure 1 shows that compared to the tumor (T1) sample, the paired normal mucosa (N1) sample contained two amplified bands representing two different alleles: One paternal and another maternal, and no allele loss was scored when comparing the normal and tumor DNA. Allele loss was detected from case 2 (N2, T2) and case 3 (N3, T3), showing the loss of the top band as related to that of the normal tissue.

### Relationship between LOH and prognosis

Of the 58 colorectal carcinoma cases, 19 patients died and 39 were still alive within five years, with a 5-year survival rate of 67.2%. The 5-year survival rate in patients with and without LOH of *DCC* gene microsatellites was 44.4% (8/18) and 77.5% (31/40), respectively ( $P$

< 0.05).

### Relationship between LOH and differentiation or Dukes' stage

The positive rates of well-, moderately, and poorly differentiated colorectal adenocarcinoma were 25.0% (4/16), 31.4% (11/35), and 42.9% (3/7), respectively, in the LOH-positive cases, and 9.1% (1/11), 30.0% (9/30), and 47.1% (8/17) in Dukes' stage A, B, and C, respectively. No statistically significant correlations were found between LOH and differentiation or Dukes' stage.

## DISCUSSION

Huang *et al.*<sup>[2]</sup> reported LOH of *DCC* gene microsatellites in 33% (7/26) of colorectal adenocarcinoma cases, but they studied a small number of cases and no follow-up data. The frequency of LOH of *DCC* gene microsatellites in our study was similar to theirs, and our results were also concordant with theirs in terms of the relationship between LOH and differentiation or Dukes' stage, which could be attributed to the small sample size in both studies. According to our follow-up data, LOH of *DCC* gene microsatellites might be closely related to the 5-year survival rate of patients with colorectal adenocarcinoma. Thus, we believe that when combined with traditional prognostic indicators, LOH of *DCC* gene microsatellites might be a new predictive marker of colorectal adenocarcinoma prognosis; however, a large number of cases are needed to confirm it.

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