Reviewers's report

Title: Tumor Biology of Rectal Cancers in Young Patients

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Version: 1 Date: 22 Jul 2002

Reviewer: Dr Xiao-Feng Sun

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after discretionary revisions

July 22, 2002

Comments and suggestions:
The authors investigated DNA ploidy, MSI, mutations of KRAS and CTNNB1, as well as the protein expression of p53, Beta-catenin, MLH1 and MSH2 in 30 rectal cancers diagnosed before age 50. Their main findings are that MSI was detected in a small fraction of the tumors, however, when MSI presented it strongly indicated an underlying HNPCC-causing mutation, and other mechanisms than HNPCC thus cause rectal cancer in the majority of young patients. The results are interesting and the discussion is acceptable. The manuscript is well written. After alterations it would be acceptance for publication.

1. TITLE PAGE:
The title is too broad. It would be better to make it more specific or provide a subtitle. "1" and "2" should be added to institutional affiliation.

2. ABSTRACT:
An abbreviation, MMR should appear directly after the mismatch repair on the line 11.

3. BACKGROUND:
A reference needs to be cited in the end of the first sentence. The last sentence of the first paragraph is too long, it would be better to split it up.

4. PATIENTS
There are 12 patients in Dukes C and 5 in Dukes D tumors (line 3) but why did 5 patients have metastasis (line 12)? "Five", instead of "5" patients (line 12), should be used according to the English writing rule.

5. METHODS:
It is necessary to indicate how negative controls and positive controls were performed during the IHC. The authors described that "nuclear p53 staining... was classified as positive if 5% of the tumor cell nuclei were stained", did they consider the intensity? If not, figure 1c shows more than "10% of the tumor cells".

6. RESULTS
It is interesting to see if biological variables analyzed in the present study are related to differentiation, stage and survival although there is a small number of the cases. Legends to figures: Fig.1 b) I can not see clear "normal crypts" (stromal components present), if there are, please indicate them. Otherwise "normal crypts" should be omitted.

7. DISCUSSION:
The first sentence of the second paragraph is unclearly presented, for examples, % of an unselected series of rectal cancer should be presented. A "->" should be used at glycine-alanine on page 11.

8. OTHERS:
K-RAS should be changed to KRAS.
Please carefully check English, for example, on the line 14 of page 11 "have" should be "has".

Competing interests:
None declared.