Reviewer’s report

Title: Association between cigarette smoking, APC mutations and the risk of developing sporadic colorectal adenomas and carcinomas

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Reviewer: Walter Giaretti

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Epidemiological and laboratory studies have clearly documented the health hazards related to cigarette smoking and, in particular, the risk of cancer in lung and oral cavity where cells are in direct contact with the smoke. More limited information is available on the association between cigarette smoking and the risk of developing sporadic colorectal adenomas and carcinomas (CRC), which was addressed in the present study by Mona Saebo et al.

As it is known, toxicity and carcinogenicity of tobacco are due to by-products of tobacco combustion including chemical compounds that reach the blood stream. Thus, tobacco may potentially contribute to mechanisms of CRC genesis. Unfortunately, the mechanisms of CRC genesis associated with tobacco specific compounds are not yet well known and a relatively small number of studies investigating these mechanisms using in vitro and mice models has been reported (see for example, Ye YN et al, Carcinogenesis, 2005:26:827-834).

The present study of Mona Saebo et al., aimed to investigate the relationship of a specific early event of CRC genesis, the APC mutations, with history of cigarette smoking in patients with sporadic colorectal adenomas and CRC is surely very interesting.

A few weaknesses are present, in my opinion, such as the evaluation of APC only for the MCR, the use of paraffin material, the screening at flexible sigmoidoscopy only, the limited number of adenoma cases. They are, however, a reasonable compromise in a pilot study.

Overall, this study was well conducted and well described and the results are stimulating. In particular, the authors considered case patients (45 with colorectal adenomas and 88 with CRCs), further subdivided in 2 groups with and without APC mutations, and compared them to control individuals (polyp free) according to several parameters of smoking history. A statistically significant association between smoking and colorectal cancer was found only for cases without APC mutations. This finding was in agreement with two previous studies.

Additionally, when the patients with CRC with and without APC mutations were considered (case-case subgroups), the smoking history of = 40 years was significantly associated (P=0.01) with APC mutations. This and all the other observations, which need to be confirmed in a larger study, are interesting and may suggest that smoking, APC mutations and CRC genesis are associated only for a very long history of smoking.

In conclusion, the present study was well conducted and well described and it is surely of relevant interest in cancer research.

What next?: Accept after discretionary revisions

Level of interest: An article of importance in its field
Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
'I declare that I have no competing interests'