Reviewer's report

Title: SOX2 Expression Correlates with Lymph-Node Metastases and Distant Spread in Colon Cancer

Version: 1 Date: 18 August 2011

Reviewer: Ida RK Bukholm

Reviewer's report:

The manuscript SOX2 Expression Correlates with Lymph-Node Metastases and Distant Spread in Colon Cancer by Neuman and co workers analyze the protein expression of SOX2 and nuclear beta catenin in 114 matched pairs of colorectal cancers and find that expression of SOX2 is associated with lymph node metastases and distant metastases.

Major revisions:

In a clinical practice it is important to find new markers which may be helpful in stratifying the patients in risk of relapse. The new markers should provide additional information than information which is available by histopathological examination. Finding that expression of some molecular biological parameters correlate to lymph node metastases is unnecessary information, but if the marker is associated with distant metastases without lymph node metastases, it may be important and valuable for clinical practice.

The authors should do a multivariate analyses of all samples and include lymph nodes and other histopathological parameters in the analyses and than analyze whether or not SOX2 and nuclear beta catenin is associated with distant metastases.

As it has been shown by others, there are significantly differences in nuclear beta catenin expression between rectal and colonic adenocarcinomas. If this is also true for SOX2 is not known. Authors should therefore analyze impact of SOX2 and nuclear beta catenin proteins both in colonic and rectal adenocarcinomas separately.

Most interesting group of patients is stage 1 and II patients (without lymph node metastases). Authors should perform analyses on impact of SOX2 and beta catenin separately for this group. Could SOX2 expression be a factor which could be used inplanning adjuvant chemotherapy or not in stage 1 and II crc patients?

Expression level of these proteins should be correlated to expression in normal mucosa of the same intestine, and cut off value should be according to expression level in the normal intestine mucosa from same patient.

Suggestions for revision:

Regression analyses for distant metastases where all known histo pathological risk factors are included for colonic and rectal carcinomas separately.
Do immunohistochemistry for SOX2 and beta catenin in matched normal mucosa for all patients and use cut off value according to expression level in the normal mucosa?
Exclude statistics analyses on 8 patients with co expression of SOX2 and beta-catenin

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, and I have assessed the statistics in my report.

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