Reviewer's report

Title: Prognostic impact of three immunohistochemically detected markers of neuroendocrine differentiation in prostate cancer

Version: 1 Date: 1 May 2008

Reviewer: Ruoqian Shen

Reviewer's report:

Neuroendocrine (NE) differentiation in prostate cancer has gradually been recognized as one of the possible mechanisms in prostate cancer progression. Therefore, analysis of the expression of NE markers in the patient samples possesses clinical significance. However, the weakness in the manuscript mentioned below greatly reduced reviewer’s enthusiasm.

1. In “Introduction”, the authors used the statistic data in 2006 (page 3). As it is 2008 now, it is better to cite the statistic data in 2007.

2. Some sentences are unclear, such as in “Results” “As a median follow up --- patients 21---”(page 7). It should be corrected as 21 patients. Some sentences are redundant, such as “for about 33% of incident cases” (page 3) and “about 33%of all new cases” (page 8).

3. In page 9, the sentence “In benign tissue, CgA expression correlated, while we could not demonstrate correlation to NSE or CgA to NSE expression” is unclear.

4. The authors indicated that “--- current evidence suggests that it has an influence on prognosis related to hormone resistant tumors or a role in the conversion to a hormone resistant phenotype”. However, the authors did not show any detailed analysis on the expression of CgA, NSE and SYN in patients with or without anti-androgen (or androgen withdrawal) therapies.

5. There are numerous reports demonstrated that elevated levels of chromogranin A and NSE were detected in blood samples of prostate cancer patients. Nevertheless, the authors did not show any corresponding data of the levels of CgA, NSE and SYN in the blood samples of these patients in supporting their results from tissue sections.

6. These tissue staining pictures are poor. Also in these representative pictures, there are no arrows showing the positive staining regions. Figure legends are too simple.