Reviewer's report

Title: The p300/CBP-associated factor modulates androgen receptor-regulated transcriptional activity and cellular growth in cultured prostate cancer cells

Version: 1 Date: 1 February 2012

Reviewer: Longgui Wang

Reviewer's report:

This manuscript describes regulation of p300/CBP-associated factor (PCAF) on androgen receptor (AR)-mediated transcriptional activity and cellular growth in prostate cancer (PCa) cells. The study showed that PCAF was upregulated in several PCa cell lines as well as in tumor tissues from patients with PCa. Upregulation of PCAF promoted ligand-induced AR transcriptional activation and cellular growth in LNCaP cells. Targeting 3'-3'-UTR of PCAF mRNA by miR-17-5p triggered its translational suppression and RNA degradation. Increased expression of PCAF in LNCaP cells was also associated with downregulation of miR-17-5p. In addition, PEITC, a chemopreventive agent of PC downregulated PCAF, inhibited AR transcriptional activity, and cell growth in LNCaP cells. Therefore authors conclude that 1) PCAF acts as a co-activator for AR and promoter recruitment of PCAF enhances transactivation of AR regulated genes in PCa cells; 2) Upregulated PCAF in PCa cells may be associated with downregulation of miR-17; 3) PEITC suppresses PCAF expression and inhibits AR signaling in PCa cells; and 4) PCAF modulates AR transcriptional activity and cellular growth in human PCa cells and could be a target for therapeutic intervention. However, these conclusions are not fully supported by the experimental data represented in this manuscript.

1. The protein level of PCAF in Fig 1A seems not in parallel with mRNA level in Fig 1B. Is there any possible explanation? No method of statistical analysis was given, and it is not clear how many independent experiments were performed. In addition, it is hard to believe there was a statistically significant difference of mRNA level, in particular between PrEC and LNCaP (Fig 1B).

2. It seems that both pCX-PCAF and PCAF siRNA worked very well (Fig 2A), however only minimal decrease or increase of PSA mRNA were seen in Fig 2B.

3. Data from Fig 2E showed that pCX-PCAF itself stimulated LNCaP cell growth in the absence of DHT. This result suggests that stimulation of prostate cancer cell growth by PCAF is not necessarily via AR.

4. There is a considerable difference of protein level of PCAF in LNCaP between Fig 1A and Fig 3D, is there any possible explanation?
5. No data support the statement on page 9, beginning at line 16 “Cells transfected with the empty vector or treated with the non-specific scrambled siRNA showed no changes in DHT-induced PSA luciferase activity”.

6. The manuscript requires editing.

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

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

I declare that I have no competing interests