Reviewer's report

Title: Membrane testosterone binding sites in prostate carcinoma as a potential new marker and therapeutic target: Study in paraffin tissue sections

Version: 1 Date: 1 March 2005

Reviewer: Craig Robson

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General
The manuscript by Dambaki et al examines the expression of membrane androgen receptors in archival prostate material. The results suggest that increased expression of membrane androgen receptors may be a marker for more aggressive tumors.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

It is unclear in the manuscript whether the authors are suggesting that the membrane androgen receptor protein is distinct from the classic intracellular androgen receptor protein. This needs to be made clear.

Some confusion exists in the designation of membrane androgen receptors (mAR) as this implies that these receptors are identical to androgen receptor (AR), whereas the probe used, testosterone conjugated to FITC, detects protein that binds androgen. This may or may not be a receptor. For example, could it be membrane bound 5-alpha reductase? In fact the authors report that the prostate cell line, DU145, does not express AR but does express membrane androgen receptors, suggesting that the two proteins are distinct. Would Membrane Testosterone Binding Protein be more appropriate?

Would it not be expected that cyproterone acetate block all AR sites, whether intracellular or membrane bound?

Results
Validation of the method: Data is referred to for Fig 1 that includes both BSA-FITC and Testo-BSA-FITC in the absence of BSA. Figure 1, however, only includes images for Testo-BSA-FITC w/o BSA and w/o cyproterone acetate. If this data is new to the previous methodology outlined in BMC Clin Pathol (2003, 3:1) then it needs to be shown. Otherwise this Figure does not need to be included.

Membrane androgen receptors are related to the gravity of the disease. For this section and Fig 4, more detail needs to be provided for the numbers of patients in each Gleason Score Group.

The manuscript would be strengthened by inclusion of confocal image for section alongside an image from a conventional fluorescent microscope. Also a 3D analysis from the confocal images should reveal the extent of localisation in the cell membrane.

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Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the
author can be trusted to correct)

P6 Need to detail length of time exposed to cyproterone acetate and when used as a blocking agent.

P7 ‘as the proposed method relays on’ … ‘as the proposed method relies on’

P7 ‘The method presented above was the conclusion of our studies’ … What does this mean?

P7 ‘annihalated’ …. ‘eliminated’

P8 – Ninety eight per cent of hyperplasias were negative for mAR’. The data in Fig 3 suggest it is more like 90%, which is correct.

P8 ‘and survival.’ …. ‘and survival.’

P9 ‘Slight only wavering of intensity’ .. ‘Small fluctuations in intensity’

P20 Legend to Fig 1, need to switch ‘upper’ and ‘lower’

Discretionary Revisions (which the author can choose to ignore)

General improvement in English

What next?: Accept after minor essential revisions

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: No

Declaration of competing interests:

I declare that I have no competing interests