Author's response to reviews

Title: Novel associations of UDP-glucuronosyltransferase 2B gene variants with prostate cancer risk in a multiethnic study

Authors:

Adriana C Vidal (adriana.vidal@duke.edu)
Cocoa Tucker (ctucker6@eagles.nccu.edu)
Joellen M Schildkraut (joellen.schildkraut@duke.edu)
Ricardo Richardson (mrrichardson@nccu.edu)
Megan McPhail (megan.mcphail@duke.edu)
Stephen J Freedland (steve.freedland@duke.edu)
Cathrine Hoyo (cathrine.hoyo@duke.edu)
Delores J Grant (dgrant@nccu.edu)

Version: 2
Date: 31 October 2013

Author's response to reviews: see over
October 31, 2013

Dear Dr. Dafne Solera
Executive Editor
BMC Cancer

We thank the reviewers for the thoughtful comments that have greatly improved our manuscript. Responses are detailed below. In the main manuscript changes to the text are highlighted in yellow.

Reviewer 1.

Minor essential revisions.
Correct 10page middle, (34) -----> [34]

Response: We corrected this error.

Reviewer 2.

Comment 1. Despite small numbers. I am interested in seeing some analysis trying to tease apart whether grade or race is the more important factor.

Response: We evaluated the association between the SNPs and prostate cancer grade, with and without adjusting for race. The magnitude of the association changed little (e.g. for rs9994887 from OR=2.54, 95% 1.41-4.61 to OR=2.27, 95% 1.24-4.14) when race was added into the statistical models. However, when stratifying by race because confidence intervals were wide, largely due to the small sample size, the findings were uninformative. It certainly will be instructive to use large data sets such as MADCAP to examine these associations. These plans are underway. Nonetheless, our results suggest that at least for the functional SNPs rs4148269 and rs3100, the association with high grade prostate cancer risk may be higher in African American men. Given that, overall, African American men are generally diagnosed with more aggressive prostate cancer tumors (Kim et al., Prostate Cancer Prostatic Dis 2001;14:262-5), presumably due to genetic predisposition, it is very likely that these functional SNPs play an important biological role. We hypothesize that the functional SNPs rs4148269 and rs3100 are associated with high grade prostate cancer in African American men.

Comment 2. Also, did you run the analysis with both rs4148269 and rs3100 in the same model to see if one has a stronger effect?

Response: We had not. We re-ran analysis and added both rs4148269 and rs3100 into a refined model. However, since these SNPs are highly correlated ($\rho=0.91$), as seen in Table 5, and the sample size is relatively small, they destabilized the model, leaving the OR for one of them undefinable. To address this comment, on page 11 of the Results section we added the following: “UGT2B15 variants rs4148269 and rs3100 were also strongly correlated (r^2 = 0.85, p < 0.0001). Including both SNPs into the same regression model to evaluate whether one SNP would have a stronger association with PC risk did not yield additional insights.”