Reviewer’s report

Title: FGFR4 Gly388Arg polymorphism contributes to prostate cancer risk: A meta-analysis of 2618 cases and 2305 controls

Version: 1 Date: 29 March 2010

Reviewer: Micah Hemani

Reviewers report:

Dear Dr. Makarov,

Thank you for the opportunity to review the article titled “FGFR4 Gly388Arg polymorphism contributes to prostate cancer risk: a meta-analysis of 2618 cases and 2305 controls.” Please find my comments below:

These authors sought to further explore the relationship between a specific polymorphism in the FGFR4 gene and the incidence of prostate cancer by performing a meta-analysis using six previously published case-controlled studies. They found that overall the likelihood of prostate cancer increased by 17% if the Arg388 allele was present. This relationship between a specific gene polymorphism and prostate cancer was present among Caucasian and Asian populations but not among the African-American population.

1. Major Revisions - The authors include limited demographic and tumor-specific characteristics of the cases and controls included in their meta-analysis other than stating “all the studies used frequency-matched controls to the cases by the age, sex or ethnicity, and the distribution of genotypes in the controls was consistent with Hardy-Weinberg equilibrium in all studies.” This additional information is important in order to determine if the increased likelihood of prostate cancer conferred by this gene polymorphism is in fact clinically relevant and to avoid the introduction of unnecessary bias. Although the authors state that this gene polymorphism has been associated with aggressiveness of prostate cancer, this conclusion is not supported by the data in this meta-analysis. A review of the studies included in this meta-analysis reveals that additional clinical and pathologic parameters are available for inclusion.

2. Major revisions - In addition, more information about the length of follow-up in these studies as well as how and why these patients were diagnosed with prostate cancer (and ruled out for prostate cancer) is needed in order to make a conclusion about this polymorphism and the incidence of prostate cancer. As the authors correctly point out, it is unclear how many patients in the control arms of these studies either have occult prostate cancer or will ultimately develop prostate cancer. In this meta-analysis, this is particularly important since a review of table 2 suggests that statistical significance is somewhat tenuous.

I do believe, however, that the findings of this meta-analysis are worthy of publication and as the authors suggest that they should stimulate a larger more
in depth analysis of FGFR4 Gly388Arg as a significant risk factor for prostate cancer among certain ethnic groups.

Sincerely,

Micah Hemani

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests