Reviewer’s report

Title: O6-Methylguanine-DNA methyltransferase protein expression by immunohistochemistry in brain and non-brain systemic tumors: systematic review and meta-analysis of correlation with methylation-specific polymerase chain reaction

Version: 1 Date: 12 October 2010

Reviewer: Alexander Dobrovic

Reviewer’s report:

Loss of MGMT activity is likely to underlie much of the sensitivity to temozolomide and other alkylating agents in brain and other cancers. In this communication, the authors have performed a review of the literature and a meta-analysis of the correlation between two methods determining absent MGMT function; promoter methylation as measured by methylation specific PCR (MSP) and immunohistochemistry.

Important methodological problems seem to exist with both assays. MGMT IHC does not have well defined cut off values between positive and negative. The non-quantitative nature of MSP is a major problem. However, as the authors mention, more quantitative methylation assessment methods will need validation.

* Minor Essential Revisions

The authors do not mention another important confounding factor. Low levels of methylation are present in the normal tissue of certain individuals in particular those with the T allele of the rs16906252 polymorphism. This may lead to false positive calls for methylation of the tumour.

In addition, further false positives may arise because of poor primer design, insufficiently stringent reaction conditions and incomplete conversion by bisulfite.

The second sentence of the abstract urgently needs revision.

Typos that need to be corrected:
"Cutt-off" (table 1)
polyclonal (table 2)
The l of monoclonal(l) is often on a new line in the tables.

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:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.