Reviewer’s report

Title: Prognostic prediction of glioblastoma by quantitative assessment of the methylation status of the entire MGMT promoter region

Version: 1 Date: 3 June 2014

Reviewer: Alexander Dobrovic

Reviewer’s report:

Major Compulsory Revisions:

The biggest flaw in this MS is that while the authors had the fortune to work with frozen tissues, the majority of diagnostics is done on FFPE DNA. Thus in the nested PCR used for the next generation protocol, the outer primers amplify a PCR product size of 289 base pairs which is not optimal for FFPE DNA which is often highly fragmented. A recommendation of a region of 150bp or shorter thus should be made.

Minor Essential Revisions:

MGMT should be italicised when referring to the gene.

The sentence “Only cluster 1 and cluster 4 (p=0.00491) and clusters 2 and 4 (p=0.0204) had statistically significant associations with PFS (Figure 1C).” should be rewritten as it is misleading as it stands.

Discretionary Revisions:

In the statement “we built a classifier to predict the malignancy of GB”, outcome might be preferable to malignancy.

It would have been useful to mention the MGMT SNP promoter SNP in the context of false positive MSP results. E.g. see McDonald, et al. The T genotype of the MGMT C>T (rs16906252) enhancer single-nucleotide polymorphism (SNP) is associated with promoter methylation and longer survival in glioblastoma patients Eur J Cancer (2013) 49 2 360-8

Although the authors state “It would be preferable to utilize information from all methylation sites.” their results show that specific regions are the best predictors of OS.

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, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests.