Reviewer’s report

Title: Enhancement of the Radiosensitizing Effect of Temozolomide: Targeting EGFR-associated Signaling in Malignant Glioma Cells

Version: 1 Date: 29 June 2013

Reviewer: Stefanie Galban

Reviewer’s report:

In this report, Choi and colleagues describe studies in a panel of GBM cell lines supporting the notion that counteracting pro-survival signals stemming from mutated EGFR may benefit overall therapeutic outcome when combined with standard of therapy (TMZ and radiotherapy). More specifically, the authors propose that targeting the PI3K/mTOR pathway or ligand-independent modulation of HSP90 by direct inhibition or epigenetic modulation through HDAC inhibition may improve therapeutic outcome for GBM patients.

Major revisions

While potentially important observations were made in this in depth analysis, it remains unclear what GBM subtype patient population may benefit from such combination treatment. The radio-sensitizing effects for all investigated treatments were clearly demonstrated by investigating effects on DNA damage, cell death, autophagy, senescence, invasion and migration. As indicated in the title the main focus of the study was to target EGFR-associated signaling due to the lack efficacious EGFR targeting therapies. The authors chose to investigate three GBM cell lines: U251, U87 and T98G but it remains unclear to the reader if these are EGFR mutant cell lines and whether EGFR mutated cell lines would be more or less responsive to targeting PI3K/mTOR or HSP90. Other preclinical studies have demonstrated efficacy of targeting PI3K/mTOR in combination with standard therapy for GBM e.g. in PTEN wt or PTEN mutant models. Beyond the discrepancy between title, choice of cell lines and lack of indication which GBM subtype might benefit from such therapy, the scientific presentation and experimental evidence was felt to be typical of papers published in BMC.

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