Reviewer's report

Title: The NF-kappa B inhibitor celastrol could enhance the anti-cancer effect of Gambogic acid on oral squamous cell carcinoma

Version: 1 Date: 23 January 2009

Reviewer: Richard Yaacov Lawrence

Reviewer's report:

Summary

The authors demonstrate that while gambogic acid induces cell kill it also induces NFkB. NFkB is though to promote cell survival. They demonstrate that the addition of celastrol to gambogic acid both decreases NFkB induction and increases cell kill – speculating that this is the mechanism. I was intrigued by their results, but felt that they were not solid enough. The experiment needs to be repeated in multiple cell lines and some more convincing means used to prove that NFkB inhibition is the mechanism of synergy.

Poor English and editing

e.g.
Page 4 line 3: instead of ‘combined treatment’ write ‘chemoradiation’

Page 4 line 14 ‘we investigated and proved’ write ‘we demonstrated’

Page 8 ‘to insure reproducibility’ write ‘ensure’

# Minor Essential Revisions
Quantify apoptosis demonstrated in figure 2 (numbers on FACS analysis unreadable)

# Major Compulsory Revisions
Only one cell line used. The results should be repeated in a second cell line.

Page 9 ‘The interaction effects of celastrol and GA were considered highly significant (P < 0.01) by the factorial ANOVA test.’ This sentence is vague – what exactly is being compared? Which concentration of celastrol is being assessed for interaction? The classical way to assess interaction of 2 drugs is an isobologram.

Page 4 line 5: ‘chemotherapy pre/post surgery improves local control and survival [in head and neck cancer].’ This is not thought to be true, and is not standard of care. Sometimes radiation (with or without) chemotherapy is combined with surgery; but not chemotherapy alone.

This paper focuses down on the specific interaction between gambogic acid and
celastrol. I would have preferred the authors to look at either:

1) the effect of multiple NFkB inhibitors (which work through different mechanisms) on gambogic acid induced cell death. This is especially true since Celastrol has multiple actions aside from NfkB inhibition (antioxidant, proteasomal activity etc).

or

2) the effect of Celastrol on multiple cytotoxic/anti-cancer agents

**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