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: 6 May 2009

Reviewer: David Stokoe

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I completely agree with both reviewers that analysis of additional OSCC cell lines is required. This is even more important when the only line being studied was generated in the lab of the author. The methods in general appear to be suitable for the conclusions generated. A major caviat regarding their conclusions is that these compounds appear to have multiple cellular targets, making direct linear conclusions suspect. For example, celastrol does appear to inhibit NF- kappaB, as judged by their gel shift assay and the p65 nuclear localization. And celastrol does increase cell killing by Gambogic acid. But it does not follow that the reason cell killing is enhanced is because of the NF-kappaB inhibition. For this conclusion to be strengthened, additional evidence would be required using more specific reagents (eg I kB that cannot be phosphorylated and degraded, or p65 siRNA).