Reviewer's report

Title: Griseofulvin stabilizes microtubule dynamics, activates p53 and inhibits the proliferation of MCF-7 cells synergistically with vinblastine

Version: 2 Date: 29 December 2009

Reviewer: Sheau-Yann Shieh

Reviewer's report:

The manuscript by Rathinasamy et al. describes the antiproliferative effect of griseofulvin (GF) on MCF7 cells and the underlying mechanism. High concentration of GF induced growth arrest and apoptosis, accompanied by activation of p53 and induction of p21. Moreover, GF disrupted microtubules, causing chromosome misalignment and formation of multinucleated cells. The author also provided evidence that GF binds tubulins at sites different from those bound by the known microtubule-disrupting drugs colchicine and vinblastine and in fact worked synergistically with the latter. These latter findings provide explanation for the action of GF and may have significant implication in its clinical application.

However, some experiment designs and their interpretations may need to be modified. Those are:

1) In Fig. 1B, a G2/M arrest was implicated, but in fact, judging from the evidence provided later, an M phase arrest is likely. To distinguish the two, the authors should also perform antibody staining using anti-phospho-Histone H3 before FACS analysis to directly assess the contribution of an M phase arrest.

2) For Fig. 1C, a kinetochore marker should be co-stained together with BubRI, as the spots appear rather large for kinetochore staining.

3) In some of the immunofluorescence studies (Fig. 1D and Fig. 2), especially under high concentration of GF, nuclear fragmentation and blebbing are evident. Were these distinguished from the multinucleated cells and how? On a related note, for a multipolar spindle, multiple spindle poles (centrosomes) can be observed, and this evidence can be obtained by staining with anti-gamma-tubulin in the immunofluorescence studies. Furthermore, multinucleation may increase the >4N population upon FACS analysis, it is not obvious whether this is the case from the data presented. The author should either provide additional evidence or rephrase the statement.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

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.