Reviewer’s report

Title: TUCAN/CARDINAL/CARD8 and apoptosis resistance in non-small cell lung cancer cells

Version: 1 Date: 21 February 2006

Reviewer: Peter Daniel

Reviewer’s report:

General

The authors report on negative results regarding the role of a putative caspase-9 inhibitor in lung cancer cells. Previous data by the John Reed lab suggested that the CARD proteine CARD8/TUCAN is an important regulator of the apoptosome and apoptosis execution. The present data show convincingly that this is not the case, at least in NSCLC cells. A few controls should be performed to corroborate these negative data.

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. In figure 4, efficient shRNA knockdown of CARD8 protein expression should be documented by Western blot analyses.
2. Figure 4: In the same vein: processing of caspase-9 and caspase-9 activity should be shown in the transfectants.
3. Figure 4: In the same system, the authors should provide evidence that the inhibition of casp9 has an impact on drug sensitivity to cisplatinum induced apoptosis. This could be done by either LEHD-fmk peptide inhibitor or a cysteiny1 mutant of casp9 that would interfere with apoptosome function. Such a positive control for caspase-9 function in this system is mandatory. APAF-1 knockdown should be considered as well.
4. Figure 4: the negative data reported here would become far more reliable if the authors could show that CARD8 knockdown does not interfere with other stimuli that trigger the mitochondrial pathway apart from cisplatinum.
5. The authors should consider to corroborate their data in a second, independent cell line system.

Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. Na3Vo4: Capitalize the „O“
2. Primers and probe for real time PCR should be indicated

Discretionary Revisions (which the author can choose to ignore)

none

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions.
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

I declare that I have no competing interests