Reviewer's report

Title: Anti-tumor effect of bisphosphonate (YM529) on non-small cell lung cancer

Version: 4 Date: 4 November 2006

Reviewer: Takeshi Yuasa

Reviewer's report:

General
I don't think this revised manuscript has been improved with the Reviewer's suggestion. I can understand establishment of the mouse model needs many efforts and many days. However, I think their in vitro work is immature.

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

In order to improve this manuscript, I think authors should demonstrate the inhibition of the prenylation of Ras or Ras related small molecule G-proteins. There are many small G-proteins and other proteins, which are activated after prenylation. Although Ras-MAPK is one of the famous proliferative signals, the upstream of the MAPK signal is not only Ras. There should be or might be Ras-dependent and Ras-independent ERK activation pathways.

Although I understand authors show p-ERK1/2 is actually inhibited by YM529, I think authors still demonstrate whether farnesylation as well as geranylgeranylation could be inhibited by YM529 or not. I think it is "essential".

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

In order to let the readers to better understand their speculation that YM529 is useful for the patients with NSCLC, I recommend authors had better show the growth inhibitory effect against the tumor bearing mice in vivo.

Discretionary Revisions (which the author can choose to ignore)

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 limited interest

Quality of written English: Acceptable

Statistical review: No