Reviewer's report

Title: Cancer cell adaptation to chemotherapy.

Version: 1 Date: 16 February 2005

Reviewer: Ryungsa Kim

Reviewer's report:

The authors described that the up-regulation of resistant genes or down-regulation in target genes might occur rapidly in human solid tumors, which was demonstrated by in vitro short term assay using biopsy samples and tumor-derived cells. Such adaptation to chemotherapy may explain the difficulty of prediction of drug resistance mechanisms on the bases of tumor type or individual tumor.

Comments:
1. From recent studies, the complexity of drug response in individual tumor may be explained with the comprehensive analysis by cDNA microarray and proteomics, which is distinguished as responders and nonresponders. These analyses may or may not include conventional drug-resistance and -target genes. Although it is still remained to be elucidated whether the conventional gene analysis or comprehensive analysis is better for predicting drug response in clinical setting, how do the authors demonstrate clinical usefulness of such genes expression analysis, even current chemotherapy regimen is used to be as combination regimen that is consisted of non-cross resistant drug.
2. On the basis of rationale for designing chemotherapy regimen, it will be important to consider target therapy for enhancing chemotherapeutic effect. Despite the fact that studies on prediction of drug sensitivity prior chemotherapy using drug sensitivity assay and gene analysis have been reported, there is no evidence of the survival benefit showing that such assay or analysis guided-chemotherapy is superior to empiric chemotherapy. These issues need to be discussed.
3. It is still unclear which is better analysis for pretreatment samples or posttreatment samples for predicting tumor response to chemotherapy. Are the analyses for both pretreatment and posttreatment samples much better?
4. The legend of Figure 3 is not found.
5. For the analysis of tumor samples, it seems that heterogeneity of tumor is a major obstacle for predicting drug response in individual tumor. How to overcome the heterogeneity of tumor for better predicting individual tumor response.
6. In the relationship between topo I and topo II, the treatment with topo II inhibitor showed the increase or decrease in topo I expression. In contrast, the treatment with topo I inhibitor decreased topo II expression. How can these findings be explained? In addition, the up-regulation of drug-resistance genes or down-regulation of target genes is different depending on tumor type, even though the same drug was exposed to tumor cells. How can it be explained?

What next?: Accept after minor essential revisions

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:
I declare that I have no competing interests