Reviewer’s report

Title: MIA is a potential biomarker for tumor load in neurofibromatosis type 1

Version: 7 Date: 29 March 2011

Reviewer: Marie Ng

Reviewer’s report:

The manuscript is nicely written. The comment/suggestion made below pertain to the statistical analysis only.

• Minor Essential Revisions
1. This may just be a documents conversion problem, but some of the p-values reported in the section “Serum concentration of MIA in NF1 patients correlates with tumor load” (p. 9) contained commas rather than decimal points.

2. Also in paragraph 3 (p. 10), the author mentioned testing the differences in MIA serum level between the groups with very low and low tumor loads excluding the outliers. It was a bit unclear if the authors simply re-ran the t-test after removing the outliers or used other procedures. It is important to note that using the t-test after the removal of outliers is technically inappropriate because the standard error estimate will be incorrect. For robust comparisons between independent groups, the authors may consider using Yuen’s test for comparing trimmed means.

• Discretionary Revisions
1. In paragraph two of the same section (p. 9), the authors mentioned that MIA serum concentration was significantly higher in NF1 patients and a p-value (P < 0.001) was reported. It may be useful to specify what statistical test was being used. Was it a two-sample t-test? Moreover, as the authors pointed out, there were quite a few outliers and a bit of heterogeneity among the groups. Did the authors take that into account by using t-test with unequal variances (i.e. Welch’s test)?

2. In paragraph 3 of the same section (p. 9), the authors reported on the ANOVA and multiple comparisons results. It may be helpful for the authors to clarify how many individual tests were being conducted as that would indicate the Bonferroni adjustment being made. Specifically, were the comparisons being done on all pairs of groups? As a minor technical note, ANOVA does not necessary have to precede multiple comparisons. Therefore, reporting on the multiple comparison results shall suffice.

3. The authors presented linear regression results on the association between the log of total internal tumor volume and MIA serum level. Have the authors considered showing the relationship in the original unit (i.e. without logarithm). That will more directly unveil whether or not the increase in MIA serum level was
a linear function of total internal tumor volume.

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.