Reviewer’s report

Title: The CTLA4 variants may interact with the IL23R- and NOD2-conferred risk in development of Crohn's disease

Version: 2 Date: 15 March 2010

Reviewer: Kazuhiro Tsukamoto

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COMMENTS:

1. In Table 1a, the gender ratio of 482 healthy control subjects was not matched to that of 333 Czech CD patients. Chi-square test indicates that there is a statistically significant difference in the gender ratio between CD patients and control subjects at P value of less than 0.0001. Since this study has a selection bias by selecting healthy control subjects, authors should perform multivariate logistic regression analysis using gender and polymorphisms of CTLA4 as variable factors in order to investigate whether these two factors contribute to the pathogenesis of the onset of CD. Because, it is important to evaluate environmental backgrounds between patients and control subjects on an association study by case-control study.

2. In Table 1b, there is a discrepancy between text of this manuscript and Table 1b. The authors described "... who developed CD under or at the age of 18 years and were diagnosed ..." in Line 5 of Page 7 in the "Methods" section. In Table 1b, however, CD patients were divided into three groups according to the age at diagnosis. For example, A1 group involves the CD patients under 17 years at diagnosis. A2 indicates those at 17 to 40 years at diagnosis. Which is true, 18 or 17 years?

3. It is very difficult to understand Tables 3a and 3b. Could you show us easier and simply?

4. The P value should be added in Table 4.

5. In the "Discussion" section, authors should explain in more details why the polymorphisms of CTLA4 were associated with early onset of CD as well as those of NOD2 or IL23R.

6. In the last sentence of Page 12 in the "Discussion" section, "... genetic background between Chinese and Czech populations differs markedly." was wrong. Authors should change "Chinese" to "Japanese", because Machida reported in the Japanese population (see Ref. 19).

Level of interest: An article of limited interest

Quality of written English: Needs some language corrections before being
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.