Reviewer's report

**Title:** Protective effect of a rare genetic variant in the hypoxia inducible factor-1 alpha gene on type 1 and type 2 diabetes

**Version:** 1  **Date:** 24 March 2009

**Reviewer:** Yukio Horikawa

**Reviewer's report:**

In this paper, Nagy et al performed an association study of one SNP of the HIF-1# gene (rs 11549465) with type 1 and 2 diabetes mellitus in Caucasians (Hungarian). They found a statistically significant decrease in frequencies of the CT and TT genotypes as well as in the T allele frequencies in type 1 and 2 diabetic patients. They conclude that the rare variant in the HIF-1# gene is associated with the occurrence of type 2 diabetes. They also demonstrate that the rare variant of HIF-1# (rs 11549465) contributes to the development of type 1 diabetes, suggesting a possible overlap in the pathomechanism of type 1 and type 2 diabetes.

However, there are several considerations to be addressed before the paper is suitable for publication.

**Major revisions**

1. In Methods section, the authors should show the power estimation for this case-control study of rs 11549465, which has a relatively small sample number. Judging from the genotyping data, the total number of this study is 890, not 900.

2. In Table 2, the authors should show p-values of HWD for genotyping of case and control, respectively. They also should perform logistic regression analyses with adjustment for at least age, sex, and BMI, and show odds ratio values with 95% confidence intervals.

3. The authors should show the functional analyses data for the mutant of HIF1A under either normoxic or hypoxic condition, even though it did not reach statistically significant differences.

**Minor revisions**

1. In Methods section, rather than Abstract, the authors should mention the name of the enzyme used for genotyping.

2. The authors should mention whether any polymorphisms other than that of the HIF-1# gene is reported to be associated with both type1 and type 2 diabetes.

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

**Quality of written English:** Needs some language corrections before being
Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.