Reviewer's report

**Title:** Circadian gene expression and impact of iduronate-2-sulfatase treatment in human fibroblasts from Hunter syndrome

**Version:** 1  **Date:** 2 July 2013

**Reviewer:** Kun-Ruey Shieh

**Reviewer's report:**

**Major Compulsory Revisions**

In this study, Mazzoccoli and colleagues have studied that circadian gene expression in human fibroblasts from Hunter syndrome with iduronate-2-sulfatase (elaprase) treatment for 24 or 144 hours. According to the functions of detective gene expression, the authors found 5 clusters of genes are related to the impacts of Hunter syndrome and iduronate-2-sulfatase treatment. These findings are interesting; however, there are some concerns to be answered or revised by the authors.

**Major Comments:**

1. Figure 1 and 2 were the same. This is unpredictable and unprofessional mistake.

2. Some important rationales were still needed to provide. Especially the specimens were fibroblasts. For example, why or how the changes of gene expression of hypoxia-inducible factor in the cardiovascular system (cluster 1) are important? Why or how the changes of gene expression of liver development (cluster 2) are important? Why or how the changes of gene expression of adipogenesis pathway (cluster 5) are important?

3. Due to the effects of iduronate-2-sulfatase were temporary and fade, the authors should provide more information about the conditions of two subjects with Hunter syndrome. For example, did these subjects take the iduronate-2-sulfatase (elaprase) treatments? Were good or ill for these subjects? Could these changes of gene expression as the predictable tools for therapeutical or curing indices?

**Minor Comments:**

1. Please indicate the full name at the first time before using the abbreviation. For example, NGS.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**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.