Reviewer's report

Title: "Genotype-first" approaches on a curious case of idiopathic progressive cognitive decline

Version: 2
Date: 22 August 2014

Reviewer: Yiran Guo

Reviewer's report:

The authors present a Chinese family with very rare neurological disease Sanfilippo syndrome (mucopolysaccharidosis IIIB) where a "genotype-first" approach with whole exome sequencing followed by Sanger validation and functional experiments identified known compound heterozygous mutations in NAGLU, and then made the correct diagnosis. Although the idea is not new, it is novel to put it into use in the context of developing countries with limited well-trained medical geneticists.

Major Compulsory Revisions
1. Please explicitly indicate in the abstract that both mutations in the NAGLU gene you identified were reported previously.
2. Please provide genomic positions and dbSNP rs numbers for the two compound heterozygous mutations p.Y309C and p.R565W.

Minor Essential Revisions
1. Please reformat references according to the journal's requirements, esp. the one below
"Only articles, datasets, clinical trial registration records and abstracts that have been published or are in press, or are available through public e-print/preprint servers, may be cited"
2. Reference for ANNOVAR is not correct
3. Are "PopFreqMax database", "ClinVar" and "Protein Data Bank" publicly available? If yes please indicate URLs.

Discretionary Revisions
NA

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