Reviewer's report

**Title:** A novel MANBA mutation resulting in residual beta-mannosidase activity associated with severe leukoencephalopathy: a pseudodeficiency variant?

**Version:** 1  **Date:** 18 May 2009

**Reviewer:** Abraham - Zlotogorski

**Reviewer's report:**

**Major Compulsory Revisions**

The authors describe a novel mutation in a patient with suspected beta-mannosidosis. The clinical phenotype of the patient was reported previously (ref. 22).

The clinical and enzymatic diagnosis is questionable- The clinical phenotype of the patient is unique; spastic tetraparesis and cerebellar ataxia were not observed in previously reported patients. Except for mental retardation, the patient does not have any other clinical features to support the diagnosis of beta-mannosidosis. Residual beta-mannosidase activity was noted in patient's leukocytes, lymphoblasts and plasma and also in transfected cells. Moreover, mutant enzyme activity in transfected cells remained significantly high.

A novel homozygous mutation c.1922G>A was found. Only 57 Norwegian and 15 Palestinians controls were tested, while the patient is of Algerian ancestry.

The authors themselves pose the possibility that the MANBA missense mutation may not be the disease-causing mutation when they raise the possibility of a pseudodeficiency of beta-mannosidase.

**Minor Essential Revisions**

Page 4, second line- patient was born to and not from.

**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.