Reviewer's report

Title: Complex Aetiology of an Apparently Mendelian Form of Mental Retardation

Version: 1 Date: 5 November 2007

Reviewer: Lina Basel-Vanagaite

Reviewer's report:

General

--------------------------------------------------------------------------------

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

1. Phenotypic and laboratory examination

Since the success of linkage analysis often depends on the precise clinical description and exclusion of patients with mental retardation caused by different etiology, it is important to know how many mentally retarded individuals examined in this study underwent physical examination, karyotyping and subtelomeric rearrangement analysis. Have any of the patients been evaluated by a clinical geneticist?

Short stature and obesity have been observed in some of the individuals – what was the parental height in these patients? How many of the patients in this study had short stature and obesity? May be these patients represent a homogeneous subgroup of patients with MR caused by a mutation in a single gene? Were linkage analysis results examined on a subgroup of patients with short stature and obesity only?

Some of the patients in the original study had abnormal vision or abnormal hearing – were these patients excluded from this study?

Some of the patients in the original description of the extended family were reported to have chromosomal abnormalities (e.g. 13q+ mosaic) – were these patients excluded from the current study?

2. It is stated that "The present study included 24 individuals……including 9 mild mentally retarded individuals and 14 non affected individuals" 9+14 = 23, not 24.

While in the methods section it was mentioned that genome-wide screening with microsatellite markers was performed on 24 individuals, 25 individuals are numbered in the pedigree – which individual was not included and why?

3. It is not clear from the description in the Methods section how many individuals were examined for copy number variations. If not all were examined, how was the selection of these particular samples performed?
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

1. An additional gene causing autosomal recessive mental retardation has been recently identified (GRIK2) – this should be added in the Introduction and the reference list.

2. There is a mistake in numbering the references starting from reference 10

3. English spelling mistakes (e.g. dysmorphic and not dismorphic) should be corrected

4. Please provide a reference for the statement "genetic or inherited etiologies are implicated in two-third of cases" (Background section)

Discretionary Revisions (which the author can choose to ignore)

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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 published

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