Reviewer's report

Title: Clinical and Molecular Characterization of Ataxia with Oculomotor Apraxia (AOA) Patients In Saudi Arabia

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Reviewer: Martin Lavin

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Since Aicardi et al 1988 described 14 patients with ataxia-oculomotor apraxia (AOA) there have been multiple reports on this syndrome. Indeed it represents two forms of AOA now known as AOA1 (aprataxin deficient) and AOA2 (senataxin deficient). The present submission describes the clinical features and mutation data for 9 AOA patients from 4 Saudi families. As such it is not particularly novel but does provide further evidence for heterogeneity in AOA. They describe a novel mutation in setx in one family and the W210C mutation in Mre11, previously described, that gives rise to ataxia-telangiectasia-like disorder (ATLD). However, they do not find evidence for mutations in aptx or setx in the majority of their patients. I am somewhat concerned by their conclusion that AOA1 is not caused by mutation in aptx in Saudi patients.

Specific Comments:

1. This work is not particularly novel but it does describe one new mutation for AOA2
2. There is some interest in the observation that some of the AOA patients are not characterised by mutations in Setx, aptx or Mre11.
3. Introduction - end of paragraph 2. Refs 6 and 7 refer to the cloning of the aptx gene. They do not refer to repair of DNA breaks. There are many references on DNA repair in AOA2 cells eg. Clements et al 2004; Gueven et al 2004 etc. which should be used.
4. The conclusions in the last paragraph of Discussion are not warranted. They refer to lack of mutations in aptx in Saudi families with AOA1. It is possible that they failed to detect mutations or that these patients are part of another syndrome, not AOA1, but with clinical overlap. These possibilities should be acknowledged. It is difficult to see how another gene defect could be responsible for a disorder identical to AOA1. More likely, it is a different disorder and perhaps the clinical phenotype should be more carefully analysed.
5. There are innumerable misspellings and poor construction of English throughout the manuscript. This needs to be addressed.