Reviewer's report

Title: Rapid diagnosis of spinal muscular atrophy using High-Resolution Melting Analysis

Version: 1 Date: 30 January 2009

Reviewer: christina brahe

Reviewer's report:

The authors have developed a new method for SMA molecular diagnosis consisting in a high-resolution melting analysis and validated their method in a relatively small cohort of 55 SMA patients and 46 controls. One of my concerns is that a PCR product of 242 bp was used which comprises a rare polymorphism described by Velasco et al. (Hum Mol Genet. 1996, 5:257-263) which could alter the melting curves.

Other comments
The first sentence in the abstract “the system applied in molecular analysis of SMA is not perfect yet” is not correct since several methods for SMA molecular genetic diagnosis have been published. In particular an RFLP analysis has been described by van der Steege et al. in 1995 which is widely used, is easy to perform and is precise.

In the background the third sentence is not clear: it should be stated that: homozygous absence of SMN2 genes does not cause SMA and is found in about 5% of normal individuals. The rest of the sentence refers to patients and is also not clear; the authors should clearly indicate that in SMA patients the number of copies of the SMN2 gene is inversely correlated with disease severity.

In the second paragraph of the background the references should be clearly indicated: for example the ref of van der Steege et al. should be given for the RFLP analysis.

The references of the papers written in Chinese will not be useful for the general readership of BMC Medical Genetics.

In the discussion, “Phosporated” probably stands for “dephosphorylated”.

The conclusion of the authors is not convincing: SSCP is currently an obsolete method due to the low sensitivity and to the time-consuming procedure, which is used by a very limited number of laboratories for the diagnosis of SMA. DHPLC has a more extensive use for mutation screening rather than for SNP analysis (as well as HRMA) and probably it is not the gold standard for the diagnosis of a condition which is feasible also for first level laboratories. In the specific case of HRMA, a quite expensive instrumentation is required, although the cost of the analysis per sample is reasonable. Thus, in my opinion, the authors should present their assay as an alternative technique for the diagnosis of SMA or as an application of HRMA, but they should not stress the putative advantages which
are not evident.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

**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.