Reviewer's report

**Title:** Combined mutations of asxl1, cbl, flt3, idh1, idh2, jak2, kras, npm1, nras, runx1, tet2 and wt1 genes in myelodysplastic syndromes and acute myeloid leukemias

**Version:** 1  **Date:** 29 April 2010

**Reviewer:** Anthony Bench

**Reviewer's report:**

The authors have thoroughly assessed 129 patients with a myeloid neoplasm (65 MDS; 64 AML) for mutations within 12 genes known to carry aberrations in these diseases. Most of the mutations identified have previously been described in MDS or AML. However, few studies have carried out large scale analysis of multiple genes as in this report.

Overall, this is a well written report that represents a thorough analysis of MDS and AML patients.

Based on their results, the authors grouped the genes assessed into four classes as an extension to the two class model of leukaemogenesis previously proposed by Prof. Gilliland and others. It should be noted that the original two-hit model also included fusion oncogenes (e.g PML-RARA; AML1-ETO [RUNX1-RUNX1T1] and CBFB-MYH11).

**Major Compulsory Revisions:**

The authors admit that the four-hit model is incomplete and highly speculative. In fact, no patient carried four mutations as predicted by this model. Furthermore, the model does not take into account fusion oncogenes described above. For this model to be robust, it should be modified to include fusion oncogenes. Hence, the authors should assess an appropriate number of AML patients carrying fusion oncogenes for further mutations. This may also require the authors to specifically address genes not part of the original study (for example KIT mutations in patients with AML1-ETO or CBFB-MYH11 fusion oncogenes).

**Level of interest:** An article whose findings are important to those with closely related research interests

**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