Reviewer's report

Title: Gene profiling of the erythro- and megakaryoblastic leukaemias induced by the Graffi murine leukaemia retrovirus

Version: 1 Date: 21 September 2009

Reviewer number: 2

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This paper analyze a model for two leukemia subtypes, F.A.B M6 and M7, associated to a really bad outcome. The study by Voisin et al is based on the analysis first of the expresión signatures of the induced erythro- and megakaryoblastic leukemias after The murine Graffi leukaemia retrovirus was inoculated on the NFS mice. Once they identified specific erythroid and megakaryocytic signatures the expression of the selected genes were validated on several ways: 1) they compare the expression profiles with previous profiles of experiments inducing megakaryocytic or erythroid differentiation, and 2) the selected genes were validated by RT-PCR on murine and human leukemia cell lines.

Second, they also screened the megakaryoblastic leukaemias for viral integrations and identified genes targeted by these integrations and potentially implicated in the onset of the disease.

Major Revisions

- The strength of the paper is based on the selection of the blastic cells to perform the analysis, avoiding the noise on the expression profile generated by the surrounding cells. However, the low number of studied samples for each subtype (three for each subtype) and the absence of a control for the study of the megakaryoblastic leukemias, are clear limitations to establish conclusions. These limitations are not clearly stated on the paper.

- The good correlation of the obtained signatures with other expression studies looking for the identification of the gene expression modifications under the induction of a specific lineage differentiation, are indicated along the paper. This good correlation may be also understand as it reflects the blocking of differentiation of the leukemic cells at a specific stage, and not a reflect of the malignant phenotype. This kind of discussion is missing on the paper.

The analysis was done using unsupervised clustering of different types of leukemias, but there is not good normal erythroid and megakaryocytic cells to establish if the variations on the expression are due to malignancy or to differentiation. So, the relevance of the selected genes is difficult to understand.

- There is available data about expression profiles of Human AML-M7 (Blood. 2004 Dec 1;104(12):3679-87). It would be interesting to discuss if these model identify some of the differentially expressed genes on primary samples.
Then it would be possible to consider that the model recapitulate the expression profile observed on human leukemia primary samples and not only on cell lines and may be used to perform in vivo testing of new therapies.

- The discussion is too long, confusing, and speculative. The description of the functions of the “poorly elucidated physiological roles” should be more precise.

- The paragraphs about targeted therapy and the role of megakaryocitic genes on the immune response are a little off subject.

Minor Essential Revisions

- The title of the manuscript “Gene profiling of the erythro- and megakaryoblastic leukaemias induced by the Graffi murine retrovirus” does not reflect the performed study, as they also analyze the integration sites, looking for oncogenes associated to the malignant phenotype.

- At the introduction it will be more precise to consider erythroblastic and megakaryocytic leukemias as two different AML subtypes.

- The number of Studied animals is not included on the material and methods description

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.