Reviewer's report

Title: Combined use of expression and CGH arrays pinpoints novel candidate genes in Ewing sarcoma family of tumors

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Reviewer: Jeffrey A Toretsky

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The manuscript "Combined use of expression and CGH arrays pinpoints novel candidate genes in Ewing sarcoma family of tumors " by Suvi Savola et al. poses the question whether chromosomal copy number alterations in ESFT are linked to patient outcome and whether particular marker genes in those regions can account for a "molecular marker" specific for ESFTs.

In general the question is well defined and the authors provide evidence for the fact that copy number alterations frequently occur in ESFT patients and are linked to recurrence and metastasis and therefore to a worse overall outcome for those patients. The authors reproduce earlier data (e.g. Toshifumi Ozaki et al 2001) also showing gains in chromosomes 1q, 8 and 12 and an increase of survival in patients with <5 chromosomal aberration. Earlier studies are appropriately cited.

With the exception of the control material used, this study material is well described, and title and abstract of the well-written manuscript accurately convey what has been found.

However, in order to suggest HDGF as a molecular marker for ESFT significantly enhanced clinical sample number and biological functional data are required.

The limitation of the work is clearly stated, which is the number of cases in the study and subsequently the poor statistical power. The authors should consider broader cooperation to increase their case numbers.

Major Compulsory Revisions
1. The specifics of clinical treatment (chemotherapy/dosage/radiation) should be provided as findings are linked to outcome.

2. Regarding the putative target gene list in table 3:
Besides HDGF none of the putative target genes listed is discussed in further detail (e.g. function of the listed genes and putative relevance for ESFTs). In fact, most of them are relatively unknown genes (as the authors noted themselves), whose specific relevance for ESFTs lacks rationale from the current point of research. More detail should be provided here.

3. Regarding the putative target gene HDGF in particular:
It is not clear, why the authors focus on HDGF. To support the significance of
HDGF in ESFT the authors might want to consider investigating the effect of EWS-FLI1 on HDGF expression (e.g. upon EWS-FLI1 knock down or over expression). The selection and analysis of HDGF is not well supported in this manuscript. The role of HDGF would be better evaluated in a separate manuscript to explore the functional relevance of this over-expression in ESFT, along with an expanded number of cases to determine if this really has clinical relevance.

Minor Essential Revisions
-the inclusion of the case-number/code on the x-axis of fig 4 A and B would be extremely helpful (is the order of patients in 4A = 4B?)
-The parenthesized letters L and H in figure 4E and F should be defined, presumably they mean high and low. What are the thresholds between high and low and how was it determined?
-it is not clear whether the "4 pooled blood samples" described in the paragraph "Nucleic acid isolation" is identical with the "pool of normal tissue samples" hybridized in the expression arrays. For clarity reasons number and type of control material should be mentioned separately in each of the legends.

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

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests