Author's response to reviews

Title: Balanced re-arrangement of chromosomes 5 and 17 points to a role for sex steroid hormones and carbonic anhydrase-related protein X in chondroblastoma pathogenesis

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Author's response to reviews: see over
Dear Editor

We are grateful for the opportunity to submit a revised version of the manuscript and appreciated the comments of the 2 reviewers. We have tried to accomplish to their comments/requests and as a result of this we think the manuscript has considerably improved.

Regarding the comments of Pierre Aman, they were mainly on the language and the clarity of the message. For this purpose we have meticulously edited all the manuscript and rephrased several sentences. Furthermore we sent out the paper for professional editing by native speakers (editing certificate included in the additional material files).

Regarding the comments of Bertha Brodin:

We combined together answers to point 1 from reviewer report and point 8 from the guidelines from the editors, because they are addressing the same issue.

We acknowledge the title might have been somehow misleading, for this reason we rephrased the title as following: A balanced t(5;17) (p15;q22-23) in chondroblastoma: frequency of the rearrangement and analysis of the candidate genes.

We combined together answers to point 2 from the reviewer report and points 6 and 7 from the guidelines from the editors.

We are grateful for the reviewer’s comment and we included the quoted review (Chagin AS, Sävendahl L: Genes of Importance in the Hormonal Regulation of Growth Plate Cartilage. Horm Res 2009;71(Suppl.2):41-47) in our reference list (reference number 8) and rephrased the discussion accordingly.

3 As rightfully claimed by the reviewer we rephrased the discussion accordingly (page 15, line 3-5).

We would like to add that we never claimed that “most of chondroblastomas (we believe the reviewer mistyped chondrosarcomas for chondroblastomas) analyzed express high levels of SRD5, ER alfa and other sex hormones and this is associated to abnormalities in chr 5 or 17”.

We actually state in the discussion (page 17, lines 18-20): “We did not find a casual relationship between the presence of the translocation and changes in the levels of SRD5A1 expression.”

4 Quite some data are already available on sex-steroid role on growth plate as also reviewed in Chagin et al 2009[1]. Some observations have already been published on estrogen expression and its possible functional role in chondrosarcomas and cartilaginous tumours in general (Cleton-Jansen AM 2005 and Grifone TJ et al 2008)[2,3]. We discussed more extensively these already available data and compared our findings with the findings in growth plate and in chondrosarcoma.

Regarding experimental model for chondroblastoma, no cell lines are available form this benign cartilaginous tumours, neither in our lab, nor in the literature or in our multinational network (www.eurobonet.eu). Micro RNA array experiments are not an option given the difficulties to collect a significant number of frozen samples with enough quality. Prompted by
the reviewer’s comment we explored possible significantly differential expression in chondroblastoma versus normal growth plate interrogating the expression array dataset we previously generated (Romeo et al. 2007; Hameetman et al. 2006) [4,5]. Therefore we included a corresponding new section in material and methods (page 11, line 18-25 and page 12 line 1-2), results (page 14, line 8-13) and discussion (page 17, line 24-25, page 18 line 1-3). Among the significantly differentially expressed genes as identified by Limma analysis there was none involved in sex steroid signalling/metabolism. No significant differential expression was found when investigating group of genes/pathways with Global analysis. Taken together our findings are suggesting a similar regulation of sex steroid signaling is taking place in chondroblastomas and in the actively replicating growth plate cartilage, therefore supporting a possible pathogetical role of sex steroid signaling in chondroblastomas.

5. We acknowledge the sentence was imprecise and we rephrased as following: “Our results indicate that the characteristic multinucleated giant cells in chondroblastoma do not have the same clonal origin as the mononuclear population, as they do not harbour the same translocation. We therefore hypothesise that they might be either reactive or originate from a distinct neoplastic clone, although the occurrence of two distinct clones is unlikely..”

We hope that in its present form the paper is acceptable and look forward to see it in press.

On behalf of the authors,

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Reference List


