Genetic variants in FBLIM1 gene do not contribute to SAPHO syndrome and chronic recurrent multifocal osteomyelitis in typical patient groups

The authors analyzed SAPHO and CRMO patients for the frequency of FBLIM1 mutations. The study does not support FBLIM1 as a disease-modifying gene. The patient population is very small (which authors mentioned). There is no control group in this study. CRMO/SAPHO patients are compared to a database (FBLIM1 allele frequencies in the largest group of European control individuals (gnomAD)). The allele frequency of FBLIM1 was identical between SAPHO/CRMO patients and healthy controls from the database.

There are not many data in this study, however, it adds to the current knowledge that the allele frequency of FBLIM1 variants in SAPHO/CRMO patients was identical to healthy controls. Therefore, these variants do not seem to contribute to the disease. However, "mice null for FBLIM1 have severe osteopenia and increased osteoclast differentiation marked by increased RANKL expression in bone marrow stromal cells" (Cox et al.).

" ...functional validation of the regulatory mutation rs41310367 suggests that there may be other non-coding mutations in linkage disequilibrium with rs114077715 contributing to CRMO disease." Cox et al.

Please extend the discussion to the data of Cox et al. PLOSOne 2017. Comment on the functional assays and the observations mad in FBLIM1-null mice...

There are some minor corrections:

Abstract: …patient group of patients…. - please correct

Page7/Lane 8: Eight CRMO patients had multifocal osteomyelitis… CRMO is defined as multifocal…. CNO is the common sentence for milder forms (also unifocal)

Page8/Lane 17: ….variants was comparable… a large group…. - missing comparable to...

Suppl Table 2B: CRMO patients number 10? Should be 8 and 1 patient with unifocal CNO
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
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Not relevant to this manuscript

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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