Reviewer's report

Title: Gene network analyses point to the importance of human tissue kallikreins in melanoma progression

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Reviewer: Jaime Matta

Reviewer's report:

The article by Martins et al. presents important questions in the field of melanoma. The manuscript would benefit from stating more clearly the central question or hypothesis being tested. The methods appear to be appropriate and well described except for the following concerns: 1) The time between surgery and snap freezing of tumors is not described nor a standardized protocol for tumor collection presented, 2) How the quality of RNA used for microarray is not presented, 3) Was the diagnosis of melanoma confirmed by an expert dermatopathologist? 4) What was the false discovery rate (FDR) used as baseline to evaluate statistical significance? In addition, this reviewer has a concern; the authors describe using a customized cDNA microarray platform containing 4,608 cDNAs. Does this introduce a bias in the type of gene networks being selected and detected since apparently this study was not done using whole genome scans. This is an important concern because this reviewer found no evidence in the data of key signaling pathways which are well known to be activated in melanoma. For example the Ras---Raf--MEK---Erk cascade contributes importantly to certain cancer cell phenotypes. In 60-70% of melanoms, a close relative and functional anaalgo of Raf, called B-Raf is found in a mutated, constitutively activated form. Was this found as part of the gene networks presented in this study? Thee manuscript adheres to the relevant standards for reporting and data deposition and the discussion and conclusions are reasonable based in the data. This article may be a strong candidate for publication but the authors should first answer the concerns expressed.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have not competing interests.