Review of: "The tumour microenvironment in BRCA1/BRCA2 hereditary breast cancer and the role of epigenetics in its regulation"

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Potential competing interests: No potential competing interests to declare.

The topic is of broad interest interest; however, in order to improve the overall quality of the paper, the authors should take into consideration the following comments:

- More information should be provided regarding the effect of *BRCA1/2* PVs on tumour microenvironment and *vice versa*.
- Any reference to BRCA1/2 is lacking in the sections '4', '5' and the subsection '7.1'.
- The Title of the paper should be rephrased as "*..the role of epigenetics in its regulation*" is not clear. BRCA1/BRCA2 play an important epigenetic and transcriptional regulatory role, since they can interact with epigenetic factors and also bind to the promoters of cancer-associated genes (e.g. TWIST and VEGF); conversely, they are being regulated at the epigenetic, transcriptional and post-transcriptional level in the tumor microenvironment.
- Some parts are considered self-explanatory. For example, "*This paracrine loop is kept in control by BRCA1, which inhibits aromatase gene expression in the stromal cells. Thus, with BRCA1 PVs, there is oestrogen overproduction [30]*". The mechanism of how this paracrine loop is controlled by BRCA1 and the effect of aromatase inhibition in oestrogen overproduction. Moreover, how "BRCA1/2 PVs can enhance tumour angiogenesis"? A rather 'cryptic' answer is provided in the next paragraph: "*BRCA1 can bind to the VEGF gene promoter and suppress its activity*". In addition, further explanation is needed regarding how "*such a difference in epigenetic regulation could have implications in the tumourigenesis of hereditary breast cancer as compared to sporadic breast cancers [92]*."
- Finally, the entire manuscript should be reformatted and undergo a thorough revision for errors in syntax, grammar and style.