# 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.

In the review entitled **"The tumour microenvironment in BRCA1/BRCA2 hereditary breast cancer and the role of epigenetics in its regulation"**, the authors aimed to explore the differences in tumour microenvironment between hereditary and sporadic breast cancer and to uncover the epigenetic mechanisms that perpetuate such tumour microenvironments and hence contribute to the tumourigenesis of hereditary breast cancer (ie. the role of LSD-1 in the suppression of BRCA1 gene expression).

The aim of this review is amazing since it has been demonstrated that hereditary genetic conditions such as the autosomal-dominant Hereditary Breast and Ovarian Cancer (HBOC) syndrome, in which genes such as BRCA1 and BRCA2 pathogenic variants (PVs) are inherited, greatly increase the risks of being diagnosed with breast cancer. Moreover, breast cancers in BRCA1/2 PV carriers tend to be more aggressive and have poorer prognoses in part because these PVs influence the tumour microenvironment and facilitate tumourigenesis through their interactions with stromal cells and immune cells, promoting epithelial-mesenchymal transition and angiogenesis, and influencing oestrogen levels. In addition, BRCA1 PVs also contribute to breast cancer by exerting epigenetic effects on cells, such as DNA methylation and histone acetylation, thereafter suppressing the expression of proto-oncogenes and promoting cytokine dysregulation.

This review is interesting in order to shed light upon mechanisms that may be harnessed to fight breast cancer by acting upon the tumor microenvironment.

The review is clear, simple to read and well organized in paragraphs.

However, there are only some issues to be addressed before to consider it for publication.

In particular, the authors should add some other schematic representations of the pathways and genes involved in the molecular mechanisms they dissected as well as some tables in order to summarize the genes involved in their comments, linking them to the references they were taken from.

It would be interesting also to improve the informations about the correlation with microRNA network.

It would be interesting to add some images regarding the crystallographic structures of LSD-1 inhibitors used in breast

cancer therapy, in order to compare them and to evidencedifferences and similarities among them.

MINOR ISSUES:

There are some typing errors within the text and terms that need to be uniformed (sometimes it is reported HIF-1a and sometimes it is reported HIF-a).

The authors should add an ABBREVIATIONS Section to the manuscript in order to clarify the meaning of such acronyms reported within the text.

I think these adding will improve the value of the manuscript. I think the review may be considered for publicaton after these revisions.