Reviewer's report

Title: Breast and other cancer dormancy as a therapeutic endpoint: speculative recombinant T cell receptor ligand (RTL) adjuvant therapy worth considering?

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Reviewer: Inge Marie Svane

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Manuscript: Breast and other cancer dormancy as a therapeutic endpoint: speculative recombinant T cell receptor ligand (RTL) adjuvant therapy worth considering.

The manuscript is a hypothesis article and the authors put forward the theory that most if not all people harbour cancer cells and that growth of these cells is prevented by the primary tumour which feeds the immune system with ‘normal tissue’ signals and thereby prevents immune activation. As a consequence, the authors claim that surgical removal of the primary tumor will lead to growth of the metastases due to the loss of ‘normal tissue’.

The hypothesis that surgery disturbs tumor dormancy has previously been put forward. Based on this hypothesis the authors propose an animal model which to their opinion should be able tomake the conclusive test of the hypothesis. Furthermore, they propose a therapeutic approach using recombinant T cell receptor ligands to prevent the cancer activation.

Major Compulsory Revisions

The theory of surgical reactivation of metastasis has been discussed for years and is questioned by many. The authors do not put forward any new evidence, and especially they do not discuss alternative explanations of the phenomenon e.g. the immune suppression induced by surgery.

In general the manuscript suffers from lack of insight into the field of tumor immunology which is essential for i.e. fully understanding their own suggestion of RTL therapy. In that line, no details what so ever are given on exactly which antigens would be relevant to target by this therapy even though it is well known by tumor immunologist that exactly that issue is one of the largest problems for development of antigen specific immunotherapeutic strategies.

Also the murine tumor model needs to described and argued for in far more details if the authors state that this model is the best choice to confirm the hypothesis.

Maybe due to the authors own lack of immunological insight it is sometimes very hard to follow their argumentation and explanations.

The authors have a very relaxed attitude to the use of references leading to
over-interpretation and disturbing generalizations. Also, some of the central references used to support their theory are published in rather peripheral magazines. In conclusion, the authors lack to describe new solid evidence to back up their hypothesis, and they also fail to argue in an understandable and sufficient way for their proposal of a solution.

**Level of interest:** An article of limited interest

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

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests