TMED2 as a marker of prognosis in breast cancer [Letter]

This article was published in the following Dove Press journal:
Cancer Management and Research

Megan Catherine Schwarz¹
Silvia Allikmets²

¹Icahn School of Medicine, Mount Sinai Oncological Sciences, New York, NY, USA; ²Faculty of Life Sciences & Medicine, GKT School of Medical Education, King's College London, London, UK

Dear Editor

We thank Lin et al for their interesting study proposing TMED2 overexpression as a potential marker of poor prognosis in breast cancer.¹ While the results imply that TMED2 overexpression decreases survival rates, we are hesitant to agree with the authors' statement claiming its prognostic power until certain aspects of the study are clarified. We further propose recommendations for consideration in future investigations to maximize the potential of this study.

The authors identified and isolated two novel cell types arising from a murine breast cancer cell line, 4T1, termed sphere cells (SC) and non-sphere cells (NSCs), that differ in their morphological, differentiative, proliferative, and metastatic properties. Transcriptomic analysis showed an upregulation of 44 and 27 metastasis-promoting genes in SCs and NSCs, respectively. It is unclear why the authors chose to focus solely on TMED2, and this may represent a missed opportunity to explore a wider range of prognostic markers. Considering the restriction of all downstream experiments to TMED2, we were surprised at the lack of depth and strong causal evidence for its role in breast cancer in this paper. The authors claim that the decreased survival and increased metastatic properties associated with SCs, compared to NSCs, are a function of TMED2 overexpression. The published work does not comment on the possible influence of the other 43 pro-metastatic genes, which are also overexpressed in this cell type. Should the authors continue to examine TMED2's role in poorer survival outcomes and increased metastasis, we propose experiments that control for other factors contributing to cell phenotype; for example, knocking out or silencing TMED2 in SCs to confirm ablation or hindering of cell metastasis in vivo. Similarly, expression of TMED2 in NSCs and subsequent rescue of their ability to metastasize would provide strong evidence for the authors' hypothesis.² A recent study on TMED2 as a prognostic marker in ovarian cancer was successful in showing the causal link between its expression and function.³

Finally, we emphasize the importance of relating the authors' findings to human cancer. This study's data analysis showed that TMED2 overexpression in human samples corresponds to lower rates of survival, but only in ER-positive breast cancer. Lin et al reveal no correlations between TMED2 mRNA expression and cancer grades, lymph-node statuses, or TP3 status. Attempts at isolating SCs and NSCs from a variety of human breast cancer cells were unsuccessful. In order for the findings of this study to command stronger clinical relevance, TMED2

Correspondence: Silvia Allikmets
Faculty of Life Sciences & Medicine, GKT
School of Medical Education, King's
College London, Great Maze Pond, SE1
1UL, UK
Email silvia.allikmets@kcl.ac.uk

expression, proliferative rates, or differentiation potential of human lines could be investigated.⁴ The lack of bifurcated morphological phenotypes in these lines does not exclude them as a valuable resource in investigating TMED2 expression in human breast cancer. Another option could be to use patient-derived xenografts originating from tumors with either low or high TMED2 expression to show relevance to humans.⁵

In conclusion, the present study is an important starting point in exploring TMED2 as a potential prognostic marker in breast cancer and, with some additional considerations, could result in significant advancements in breast cancer prognosis.

Disclosure

The authors report no conflicts of interest in this communication.

References

1. Lin X, Liu J, Hu SF, et al. Increased expression of TMED2 is an unfavorable prognostic factor in patients with breast cancer. *Cancer Manag Res*. 2019;11:2203–2214. doi:10.2147/CMAR.S192949.
2. Xie JY, Chen PC, Zhang JL, et al. The prognostic significance of DAPK1 in bladder cancer. *PLoS One*. 2017;12(4):e0175290. doi:10.1371/journal.pone.0175290.
3. Shi-Peng G, Chun-Lin C, Huan W, et al. TMED2 promotes epithelial ovarian cancer growth. *Oncotarget*. 2017;8(55):94151–94165. doi:10.18632/oncotarget.21593.
4. Holliday DL, Spiers V. Choosing the right cell line for breast cancer research. *Breast Cancer Research*. 2011;13(4):215. doi:10.1186/bcr2889
5. Tury S, Becette V, Assayag F, et al. Combination of COX-2 expression and PIK3CA mutation as prognostic and predictive markers for celecoxib treatment in breast cancer. *Oncotarget*. 2016;7(51):85124–85141. doi:10.18632/oncotarget.13200.

Dove Medical Press encourages responsible, free and frank academic debate. The content of the Cancer Management and Research 'letters to the editor' section does not necessarily represent the views of Dove Medical Press, its officers, agents, employees, related entities or the Cancer Management and Research editors. While all reasonable steps have been taken to confirm the content of each letter, Dove Medical Press accepts no liability in respect of the content of any letter, nor is it responsible for the content and accuracy of any letter to the editor.

Cancer Management and Research

Dovepress

Publish your work in this journal

Cancer Management and Research is an international, peer-reviewed open access journal focusing on cancer research and the optimal use of preventative and integrated treatment interventions to achieve improved outcomes, enhanced survival and quality of life for the cancer patient.

The manuscript management system is completely online and includes a very quick and fair peer-review system, which is all easy to use. Visit <http://www.dovepress.com/testimonials.php> to read real quotes from published authors.

Submit your manuscript here: <https://www.dovepress.com/cancer-management-and-research-journal>