Letter to the editor:

IMMUNE RESPONSES DURING NEOADJUVANT CHEMOTHERAPY IN TRIPLE NEGATIVE BREAST CANCER

Ahmed Ghallab

Forensic Medicine and Toxicology Department, Faculty of Veterinary Medicine, South Valley University, Qena, Egypt, E-mail: ghallab@vet.svu.edu.eg

http://dx.doi.org/10.17179/excli2020-2869

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0/).

Dear Editor,

Recently, Axelrod and colleagues analyzed immune-related gene expression changes in breast cancer before and after neoadjuvant chemotherapy (Axelrod et al., 2020). The authors analyzed 83 breast cancer tissue specimens, among them 44 triple negative carcinomas. An interesting result was that upregulation of immune-related genes was associated with better prognosis in the triple negative breast carcinomas (Axelrod et al., 2020). Moreover, the authors studied PD-1^{Hi} CD8+ peripheral T-cells for a cytolytic gene signature. Expression of cytotoxic genes in the peripheral blood was associated with worse prognosis, which may be explained by persistent micrometastatic disease that finally leads to recurrence (Axelrod et al., 2020).

Numerous studies have analyzed the association of breast cancer with outcome, including the spontaneous course of disease and response to chemotherapy (Sparano et al., 2018; Wang et al., 2018; Finak et al., 2008; van de Vijver et al., 2002; Kwa et al., 2017). High levels of T-cell and also B-cell/plasma cell associated genes were observed in breast carcinomas with relatively good prognosis (Schmidt et al., 2008, 2012, 2018; Heimes et al., 2017) but also in other tumor types (Edlund et al., 2019; Lohr et al., 2013). In contrast, antioxidative genes (Cadenas et al., 2010) and genes associated with proliferation (Siggelkow et al., 2012; Hellwig et al., 2016; Cadenas et al., 2014) and lipid (Cadenas et al., 2019) as well as glycerophospholipid (Marchan et al., 2017; Stewart et al., 2012) metabolism are linked to worse prognosis. The current study of Axelrod et al. (2020) is of high interest, because the authors systematically analyzed tumor tissue before and after chemotherapy and clearly demonstrated the prognostic role of genes associated with better response.

Conflict of interest

The author declares no conflict of interest.

REFERENCES

Axelrod ML, Nixon MJ, Gonzalez-Ericsson PI, Bergman RE, Pilkinton MA, McDonnell WJ, et al. Changes in peripheral and local tumor immunity after neoadjuvant chemotherapy reshape clinical outcomes in patients with breast cancer. Clin Cancer Res. 2020;clincanres.3685.2019. epub ahead of print. doi: 10.1158/1078-0432.CCR-19-3685.

Cadenas C, Franckenstein D, Schmidt M, Gehrmann M, Hermes M, Geppert B, et al. Role of thioredoxin reductase 1 and thioredoxin interacting protein in prognosis of breast cancer. Breast Cancer Res. 2010;12: R44. doi: 10.1186/bcr2599.

Cadenas C, van de Sandt L, Edlund K, Lohr M, Hellwig B, Marchan R, et al. Loss of circadian clock gene expression is associated with tumor progression in breast cancer. Cell Cycle. 2014;13:3282-91. doi: 10.4161/15384101.2014.954454.

Cadenas C, Vosbeck S, Edlund K, Grgas K, Madjar K, Hellwig B, et al. LIPG-promoted lipid storage mediates adaptation to oxidative stress in breast cancer. Int J Cancer. 2019;145:901-15. doi: 10.1002/ijc.32138.

Edlund K, Madjar K, Mattsson JSM, Djureinovic D, Lindskog C, Brunnström H, et al. Prognostic impact of tumor cell programmed death ligand 1 expression and immune cell infiltration in NSCLC. J Thorac Oncol. 2019;14:628-40. doi: 10.1016/j.jtho.2018.12.022.

Finak G, Bertos N, Pepin F, Sadekova S, Souleimanova M, Zhao H, et al. Stromal gene expression predicts clinical outcome in breast cancer. Nat Med. 2008;14:518-27. doi: 10.1038/nm1764.

Heimes AS, Madjar K, Edlund K, Battista MJ, Almstedt K, Elger T, et al. Subtype-specific prognostic impact of different immune signatures in node-negative breast cancer. Breast Cancer Res Treat. 2017;165: 293-300. doi: 10.1007/s10549-017-4327-0.

Hellwig B, Madjar K, Edlund K, Marchan R, Cadenas C, Heimes AS, et al. Epsin family member 3 and ribosome-related genes are associated with late metastasis in estrogen receptor-positive breast cancer and long-term survival in non-small cell lung cancer using a genome-wide identification and validation strategy. PLoS One. 2016;11:e0167585. doi: 10.1371/journal.pone.0167585.

Kwa M, Makris A, Esteva FJ. Clinical utility of geneexpression signatures in early stage breast cancer. Nat Rev Clin Oncol. 2017;14:595-610. doi: 10.1038/nrclinonc.2017.74.

Lohr M, Edlund K, Botling J, Hammad S, Hellwig B, Othman A, et al. The prognostic relevance of tumour-infiltrating plasma cells and immunoglobulin kappa C indicates an important role of the humoral immune response in non-small cell lung cancer. Cancer Lett. 2013;333:222-8. doi: 10.1016/j.canlet.2013.01.036.

Marchan R, Büttner B, Lambert J, Edlund K, Glaeser I, Blaszkewicz M, et al. Glycerol-3-phosphate acyltransferase 1 promotes tumor cell migration and poor survival in ovarian carcinoma. Cancer Res. 2017;77: 4589-601. doi: 10.1158/0008-5472.CAN-16-2065.

Schmidt M, Böhm D, von Törne C, Steiner E, Puhl A, Pilch H, et al. The humoral immune system has a key prognostic impact in node-negative breast cancer. Cancer Res. 2008;68:5405-13. doi: 10.1158/0008-5472.CAN-07-5206.

Schmidt M, Hellwig B, Hammad S, Othman A, Lohr M, Chen Z, et al. A comprehensive analysis of human gene expression profiles identifies stromal immunoglobulin κ C as a compatible prognostic marker in human solid tumors. Clin Cancer Res. 2012;18:2695-703. doi: 10.1158/1078-0432.CCR-11-2210.

Schmidt M, Weyer-Elberich V, Hengstler JG, Heimes AS, Almstedt K, Gerhold-Ay A, et al. Prognostic impact of CD4-positive T cell subsets in early breast cancer: a study based on the FinHer trial patient population. Breast Cancer Res. 2018;20(1):15. doi: 10.1186/s13058-018-0942-x.

Siggelkow W, Boehm D, Gebhard S, Battista M, Sicking I, Lebrecht A, et al. Expression of aurora kinase A is associated with metastasis-free survival in node-negative breast cancer patients. BMC Cancer. 2012;12: 562. doi: 10.1186/1471-2407-12-562.

Sparano JA, Gray RJ, Makower DF, Pritchard KI, Albain KS, Hayes DF, et al. Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. N Engl J Med. 2018;379:111-121. doi: 10.1056/NEJMoa1804710.

Stewart JD, Marchan R, Lesjak MS, Lambert J, Hergenroeder R, Ellis JK, et al. Choline-releasing glycer-ophosphodiesterase EDI3 drives tumor cell migration and metastasis. Proc Natl Acad Sci U S A. 2012;109: 8155-60. doi: 10.1073/pnas.1117654109.

van de Vijver MJ, He YD, van't Veer LJ, Dai H, Hart AA, Voskuil DW, et al. A gene-expression signature as a predictor of survival in breast cancer. N Engl J Med. 2002;347:1999-2009. doi: 10.1056/NEJMoa021967.

Wang S, Beeghly-Fadiel A, Cai Q, Cai H, Guo X, Shi L, et al. Gene expression in triple-negative breast cancer in relation to survival. Breast Cancer Res Treat. 2018;171:199-207. doi: 10.1007/s10549-018-4816-9.