Expression of MAGE-A antigens is frequent in triple-negative breast cancers but does not correlate with that of basal-like markers

Cancer testis (CT) antigens, which are encoded by genes expressed in germline cells, silenced in normal adult tissues, and ectopically reexpressed in tumor cells, are targets of choice for cancer immunotherapy [1]. About half of the known CT antigens are encoded by genes located in the X chromosome (CT-X) and include some frequently expressed gene families, such as melanoma-associated antigen-A (MAGE-A), encoding a group of conserved proteins. The frequency of expression of CT antigens, including MAGE-A, however, is highly variable in tumors of different histological types, with high frequencies reported for some of them (e.g. melanoma, ovarian cancer, lung cancer) but not for others (e.g. colon cancer, prostate cancer).

Whereas previous studies exploring CT antigen expression in breast cancer (BC) have yielded contradictory findings, two recent papers [2, 3] have reported frequent expression of MAGE-A and other CT-X in hormone-receptor (HR)-negative BC, including triple-negative (TN) primary BC, but not in HR-positive BC. Because TN BC are generally of high grade and associated with poor prognosis and limited therapeutic options, the frequent expression of CT antigens in this tumor type offers the opportunity for a much needed new therapeutic option for these patients.

TN BC include basal-like cancers that express markers common to precursors located in the basal epithelium of the normal breast, generally referred to as stem cells [4]. It has been therefore suggested that basal-like cancers may originate from these precursors. On the other hand, it has been proposed that expression of CT antigens in cancer may identify ‘reservoir’ cancer cells with stem-like features (cancer stem cells) [1]. In addition, the presence of X chromosomal abnormalities in basal-like BC may suggest a functional link with expression of CT antigens [5]. On the basis of these concepts, it has been inferred that expression of CT antigens in TN BC may be associated with basal-like features, but no experimental data in support of this have been provided.

To explore the correlation between CT antigen expression in TNBC and basal-like associated markers, we assessed the expression of MAGE-A antigens and basal-like associated markers, including epidermal growth factor receptor, p63, CK5, and CK14, in a group of TN primary BC samples collected at the Italian National Cancer Institute (Aviano, Italy). Consistent with the recent report from Curigliano et al. [3], we found expression of MAGE-A proteins in (10/44) 23% of the samples (Figure 1). As expected, we also found a frequent expression of basal-like markers, with 80% of the TN tumors expressing at least one of them. We failed, however, to detect a correlation between MAGE-A expression and any of the markers. Thus, expression of CT antigens, although frequent in TN tumors, does not correlate with a basal-like type, indicating that the precursors and or/molecular events giving rise to CT antigen-expressing and basal-like tumors are not identical. The molecular basis for the selective expression of CT antigens in HR-negative tumors, therefore, remains to be elucidated, along with the expression of CT antigens in relation to overexpression of human epidermal growth factor receptor 2.

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**disclosure**

The authors declare no conflict of interest.

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**Figure 1.** Expression of MAGE-A antigens and of basal-like markers in triple-negative BC. Expression of MAGE-A, CK14, CK5, EGFR, and p63 was assessed by IHC staining of 44 paraffin-embedded triple-negative BC tumors, obtained at the Italian National Cancer Institute, upon written informed consent and approval by the Ethics Committee of the Centro di Riferimento Oncologico, using the mAb 6C1, L1002, XM26, 3C6, and 4A4, respectively. Tumors were scored based on the percentage of positive cells (–, 0-rare; 1, <10%; 2, 10%–25%; 3, 25%–50%; 4, >50%) and the staining intensity (A, faint; B, moderate; C, strong). An example of a tumor scored as 3C for MAGE-A expression is shown in (A) (magnification × 10) and the score of all MAGE-A-expressing tumors is summarized in (B). The percentages of tumors expressing the indicated basal-like markers within the entire cohort or among MAGE-A+ tumors is summarized in (C). MAGE-A, melanoma-associated antigen-A; BC, breast cancer; EGFR, epidermal growth factor receptor; IHC, immunohistochemistry.
references


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