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A paradigm of the complexity of B cells expressing membranous TNF-α in the tumor draining lymph nodes of breast cancer

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Membranous tumor necrosis factor-α (mTNF-α) is the membrane-bound primary form of TNF-α, mainly expressed by lymphocytes, monocytes and macrophages. It preferentially binds to TNF receptor 2, and exerts either immune stimulatory or regulatory effects in both direct and reverse signaling pathways. Herein, we investigated the expression of mTNF-α in CD19+ B cells derived from breast tumor-draining lymph nodes (LNs), and assessed its associations with breast cancer prognosticators. Mononuclear cells were isolated from 41 fresh axillary LNs and stimulated for 5 hours with PMA/Ionomycin. Cells were stained for CD19 and mTNF-α, and examined by flow cytometry. Results showed that 13±9.3% of $CD19^+$ B cells expressed mTNF-α with various intensities. The geometric mean fluorescence intensity (gMFI) of mTNF-α showed reverse correlation with the frequency of $mTNF\text{-}α^+$ B cells (R=–0.5, P=0.002). Besides, the frequency of mTNF-α-expressing B cells showed a decreasing trend in patients in N3 group (>9 involved LNs) compared with N1 (1-3 involved LNs, P=0.065), and negatively correlated with the number of involved LNs (R=-0.4, P=0.021). However, the gMFI of mTNF-α in CD19+ cells was significantly higher in N3 compared with N1 (P=0.023), and directly correlated with the number of involved LNs (R=0.3, P=0.050). Furthermore, the gMFI of mTNF-α in B cells was significantly higher in stage III compared with stage II (P=0.009). Therefore, higher frequency of mTNF-α-expressing B cells was associated with good prognostic markers, whereas the expression intensity of mTNF-α in B cells correlated with poor prognosticators of breast cancer. These data highlight the complex role of $mTNF\text{-}α^+CD19^+$ B cells in breast cancer immunity, and warrant further need for the full characterization of B cells with high or low expression intensities of mTNF-α.

Keywords: membranous TNF-α, $CD19^+$ B cell, Tumor draining lymph node, Breast cancer

Biography:

Atri Ghods is a research assistant at Shiraz Institute for Cancer Research, where she works in a lab supervised by Prof. Abbas Ghaderi and Dr. Fereshteh Mehdipour. She was graduated from university with a master's degree in Medical Immunology. Her main research area is the characterization of adaptive immune responses formed in tumor-draining lymph nodes, and their changes during cancer progression. Focusing mostly on the role of TNF-a, mTNF-a, and their receptors in breast cancer immunity, she gained expertise in various cellular and molecular biology techniques. As a young researcher, she is interested to expand her knowledge in different areas of tumor immunology.

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