



Medical, Life science

The significance of peritumoral tertiary lymphoid structures in predicting prognosis and immunotherapy efficacy in esophageal cancer

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Abstract

This study investigates the predictive value of tertiary lymphoid structures (TLS) in determining prognosis and response to anti-PD-1 therapy in patients with esophageal cancer. TLS are organized clusters of immune cells that form around tumors and possibly play a crucial role in the anti-tumor immune response; however, it is still not well understood in esophageal cancer. By analyzing surgical specimens, this research demonstrated that a higher density of TLS, particularly mature TLS containing CD138+ plasma cells, correlates with improved patient outcomes. These outcomes include better overall survival and increased effectiveness of immune checkpoint inhibitors (ICIs) such as anti-PD-1 antibodies. These findings suggest that TLS may serve as a useful biomarker for predicting both patient prognosis and responsiveness to immunotherapy in esophageal cancer.

Background & Results

Esophageal cancer is an aggressive malignancy with limited treatment options and a high rate of recurrence after surgery, contributing to poor patient outcomes. Although immune checkpoint inhibitors (ICIs) such as anti-PD-1 antibodies have introduced new treatment possibilities, their success varies between individuals. This variability emphasizes the needs for reliable predictive biomarkers that can identify patients who will benefit most from immunotherapy. In this study, 316 patients from Osaka University Hospital and Osaka International Cancer Institute who underwent curative surgery for esophageal cancer without neoadjuvant therapies were analyzed. We assessed the density and maturity of TLS in the tumor margins of specimens and demonstrated that the density and maturity of TLS rapidly elevated in early-stage cancers compared to normal and dysplasia tissues, and decreased with tumor stage. We also suggested that their higher density was linked to better immune function, as indicated by favorable nutritional immunological indices in blood tests and improved survival. In particular, mature TLS that contained a significant number of CD138+ plasma cells were strongly associated with improved prognosis. Additionally, in another subset of 34 patients who experienced recurrence and were treated with anti-PD-1 therapies, those with higher TLS density at the time of surgery had more favorable response to the immunotherapy. These results suggest that TLS, especially mature TLS, are crucial to the anti-tumor immune response and could be used as a predictive tool for both survival outcomes and immunotherapy efficacy.

Significance of the research and Future perspective

The results of this study underscore the importance of TLS as both a prognostic and predictive biomarker in esophageal cancer

treatment. Evaluating TLS density and maturity prior to surgery or immunotherapy could guide clinicians in selecting the most appropriate treatment plans, allowing for more personalized and effective care. Future research may also explore therapeutic strategies that induce TLS formation, potentially enhancing the host-immune response to cancer and improving patient outcomes. This work opens the door to novel approaches that could significantly improve survival rates and treatment success in esophageal cancer patients.



Fig 1: Morphology of Peritumoral TLS and Progression-Free Survival According to TLS Maturity in Esophageal Cancer



Fig 2: Transition of TLS Composition Cells and TLS Expression According to Anti-PD-1 Treatment Response

Hayashi, Yoshinori; Makino, Tomoki; Sato, Eiichi et al. Density and maturity of peritumoral tertiary lymphoid structures in oesophageal squamous cell carcinoma predicts patient survival and response to immune checkpoint inhibitors. Br J Cancer. 2023, 128(12), 2175-2185 doi: 10.1038/s41416-023-02235-9