# Improving immune checkpoint inhibitors' anti-tumor response and minimizing side effects

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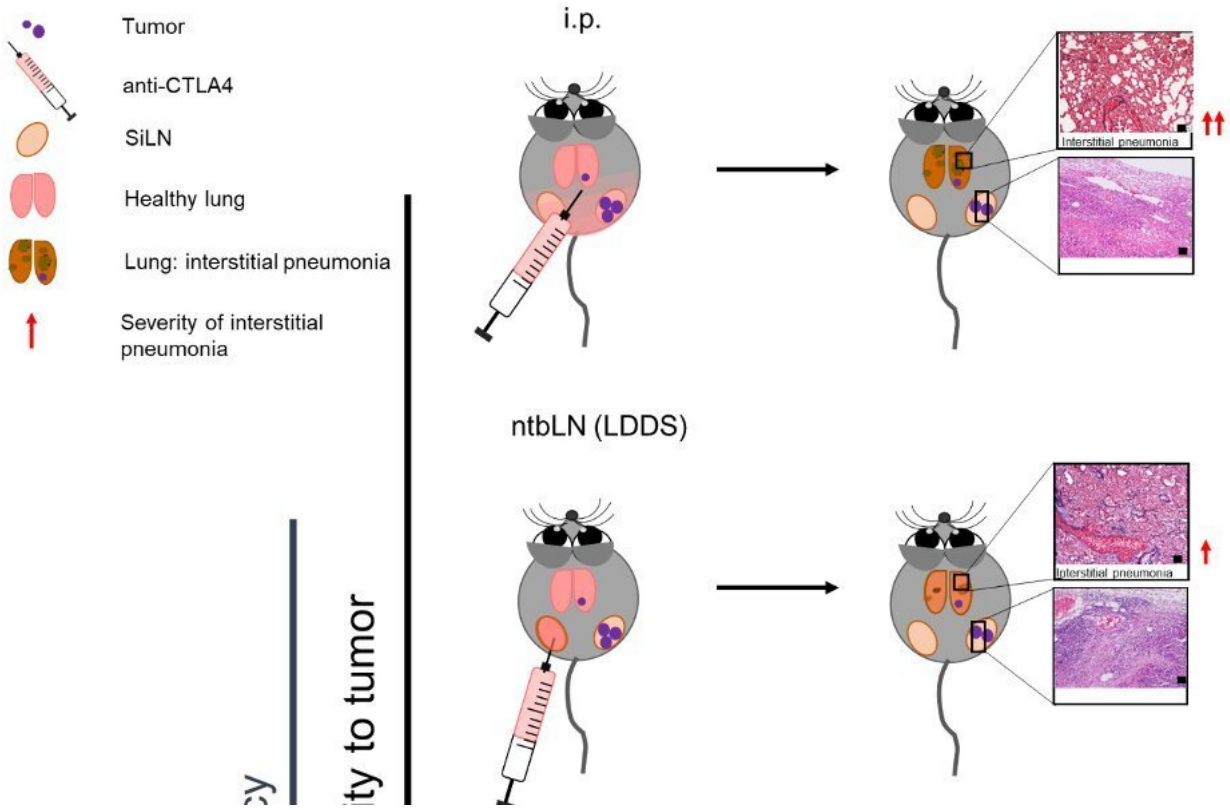


Metastatic lymph node targeted immune checkpoint blockade (ICB) elicits strong therapeutic response and ameliorates ICB-induced interstitial pneumonia. Credit: Tohoku University

Scientists at Tohoku University have discovered a novel approach that improves the efficacy of immune checkpoint blockade (ICB)—a novel form of cancer treatment utilizing immune checkpoint inhibitors (ICIs)—and minimizes the associated side effects. They demonstrated that using ICIs to target tumor-positive lymph nodes generates a robust anti-tumor response against both local and systemic metastases.

The study was published in the *Journal of Experimental and Clinical Cancer Research*.

Our immune system uses checkpoint proteins to regulate and control the activity of immune cells. But cancer cells can sometimes use these checkpoints to escape detection. ICB is a powerful immunotherapy that works to block these checkpoints and bolsters the immune system's natural ability to fight cancer, rather than targeting the cancer directly.

Yet, ICB treatment's efficacy varies from person-to-person, and it can come with some serious side effects. Medically, these are referred to as immune-related adverse events (irAEs).

The research team, which was led by Professor Tetsuya Kodama from Tohoku University's Graduate School of Biomedical Engineering, hypothesized that metastatic lymph node-targeted ICB could improve the anti-tumor response while uncoupling it from irAEs.

The researchers tested their hypothesis by using anti-CTLA4—a widely used ICI—on laboratory mice with lymph node and distant metastases. Their findings confirmed that delivering CTLA4 blockers directly to tumor-positive lymph nodes elicited a potent anti-tumor response against local and systemic metastases, prolonging the mice's chance of survival.

The cancer immunotherapeutic effect was mediated by an upregulation of functionally active T cell population in the tumor-positive lymph node

and spleen. In comparison, non-specific CTLA4 blockades elicited a weaker anti-tumor effect and exacerbated the side effects of using immune checkpoint inhibitors, particularly interstitial pneumonia.

"Our findings are significant because they provide a simple approach to enhancing the efficacy of ICB, while minimizing its associated side effects," said Kodama. "Targeting tumor-positive lymph nodes with ICB can amplify the anti-tumor response and minimize irAEs, leading to better outcomes for cancer patients."

Looking ahead, the team plans to further investigate lymphatic targeted approaches for improvement of therapeutic response in clinical trials to confirm its efficacy in humans.

**More information:** Metastatic lymph node targeted CTLA4 blockade: a potent intervention for local and distant metastases with minimal ICI-induced pneumonia, *Journal of Experimental and Clinical Cancer Research* DOI: 10.1186/s13046-023-02645-w

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