A novel therapeutic strategy for photoimmunotherapy via intratumoral delivery of antibody–photoabsorber conjugates

Department of Respiratory Medicine and Clinical Immunology, Graduate School of Medicine

Visiting Academic Staff Yuichi Adachi

Assistant Professor Kotaro Miyake Researchmap https://researchmap.jp/kotaro_researchmap?lang=en

Abstract

Photoimmunotherapy (PIT) is an emerging cancer treatment that selectively destroys tumor cells by combining a monoclonal antibody with a photoabsorber dye and irradiating the target with near-infrared light. The photoabsorber IRDye700DX (IR700) is activated only upon light exposure, achieving high target specificity with minimal off-target toxicity. However, the therapeutic efficacy of PIT *in vivo* remains limited compared to its potent *in vitro* cytotoxicity. This study aimed to enhance the efficacy of PIT by optimizing the antibody delivery route. We investigated the therapeutic potential of intratumoral administration of an anti-CD44 antibody–photoabsorber conjugate in comparison with conventional intravenous injection. Intratumoral delivery markedly improved antibody accumulation within tumors and significantly suppressed tumor growth after irradiation. Furthermore, the waiting period between administration and irradiation was reduced from 24 hours to 30 minutes without loss of efficacy, demonstrating the feasibility of a rapid, one-hour PIT protocol.

Background & Results

PIT employs antibody–photoabsorber conjugates to induce selective tumor cell death under near-infrared light exposure. Despite promising *in vitro* results, insufficient *in vivo* responses have been reported, potentially due to limited intratumoral antibody distribution. To address this issue, we evaluated the influence of administration route on therapeutic outcome using a Lewis lung carcinoma (LLC) mouse model. The anti-CD44 antibody–IR700 conjugate was administered intravenously (IV) or intratumorally (IT). Quantitative analysis revealed that IT administration achieved approximately fivefold higher antibody binding to tumor cells compared with IV injection, resulting in more homogeneous intratumoral distribution and reduced off-target accumulation in normal organs. Tumor growth was strongly inhibited in the IT group following near-infrared irradiation, with relative tumor volumes at day 7 of 4.3 (control), 2.2 (IV), and approximately 1.0 (IT). Comparable therapeutic efficacy was obtained when irradiation was performed 30 minutes after IT injection, indicating that PIT can be completed within one hour. These findings demonstrate that local administration markedly enhances PIT efficacy *in vivo*.

Significance of the research and Future perspective

This study proposes a novel therapeutic strategy for photoimmunotherapy based on intratumoral delivery of antibody–photoabsorber conjugates. By improving local drug accumulation, this approach significantly enhances antitumor efficacy and enables a rapid treatment protocol. The intratumoral injection strategy also simplifies the procedure by eliminating the prolonged waiting period required in conventional systemic administration. These results suggest that combining intratumoral PIT with localized light irradiation devices could facilitate the clinical application of photoimmunotherapy as an immediate, minimally invasive cancer treatment. Furthermore, this approach may be extended to various antibody targets and tumor types, contributing to the development of next-generation localized cancer therapies.

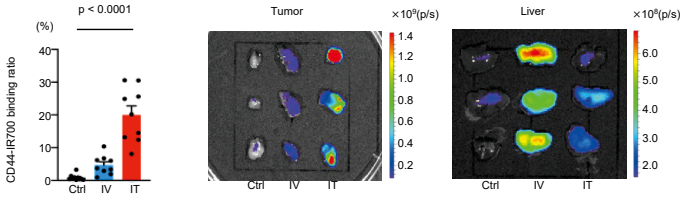

Figure 1 Left: CD44-IR700 binding percentage by flow cytometry in treatment groups without CD44-IR700 administration (Ctrl), intravenous (IV) administration, and intratumoral (IT) administration to syngeneic transplanted tumor cells. Center, Right: Distribution of CD44-IR700 in tumors and liver using IVIS imaging.

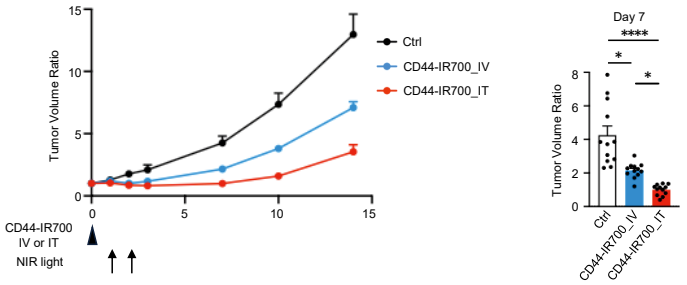

Figure 2 Effects of photoimmunotherapy via CD44-IR700 administration to syngeneic tumor-bearing mice: no treatment (Ctrl), intravenous (IV), and intratumoral (IT) administration. Changes in tumor volume ratio relative to baseline (set as 1) (left), and tumor volume ratio on day 7 (right). *:p < 0.05. ****:p < 0.0001

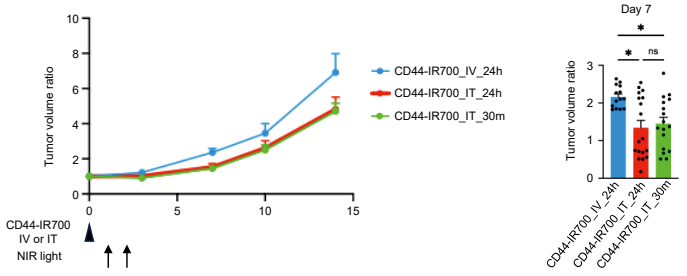

Figure 3 Effect of photoimmunotherapy following intravenous administration of CD44-IR700 to syngeneic tumor-bearing mice 24 hours prior (IV_24h), intra-tumoral administration 24 hours prior (IT_24h), and near-infrared light irradiation 30 minutes after intratumoral administration (IT_30m). Changes in tumor volume ratio relative to baseline (set as 1) (left), and tumor volume ratio on day 7 (right). *:p < 0.05.

Patent

Treatise Adachi, Yuichi; Miyake, Kotaro; Ohira, Kila et al. Enhancing the efficacy of near-infrared photoimmunotherapy through intratumoural delivery of CD44–targeting antibody–photoabsorber conjugates. eBioMedicine. 2025, 112, 105566. doi: 10.1016/j.ebiom.2025.105566

URL

Keyword photoimmunotherapy, intratumoural administration, lung cancer, antibody–photoabsorber conjugate